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- (71) Applicant (for all designated States except US): GENESIS RESEARCH & DEVELOPMENT CORPORATION LIMITED [NZ/NZ]; 1 Fox Street, Parnell, Auckland (NZ).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): WATSON, James, D. [NZ/NZ]; 769 Riddell Road, St Heliers, Auckland (NZ). STRACHAN, Lorna [GB/NZ]; 4B/94 Nelson Street, Auckland City (NZ). SLEEMAN, Matthew [GB/GB]; c/-Cambridge Antibody Technology, Cambridge House, The Science Park, Melbourn Royston, Cambridgeshire, SG8 6JJ (GB). ONRUST, Rene [NZ/NZ]; 21 Duart Avenue, Mt Albert, Auckland (NZ). MURISON, James, Greg [NZ/NZ]; 24 Calgary Street, Sandringham, Auckland (NZ). KUMBLE, Krishanand, D. [IN/US]; 2301 S Millbend Drive #706, The Woodlands, TX 77380 (US).

- (74) Agents: HAWKINS, Michael, Howard et al.; Baldwin Shelston Waters, P.O. Box 852, Wellington (NZ).
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(54) Title: COMPOSITIONS ISOLATED FROM SKIN CELLS AND METHODS FOR THEIR USE

(57) Abstract: Isolated polynucleotides encoding polypeptides expressed in mammalian skin cells are provided, together with expression vectors and host cells comprising such isolated polynucleotides. Methods for the use of such polynucleotides and polypeptides are also provided.

COMPOSITIONS ISOLATED FROM SKIN CELLS AND METHODS FOR THEIR USE

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Technical Field of the Invention

This invention relates to polynucleotides, polypeptides, polypeptides expressed in skin cells, and various methods for treating a patient involving administration of a polypeptide or polynucleotide of the present invention.

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Background of the Invention

The skin is the largest organ in the body and serves as a protective cover. The loss of skin, as occurs in a badly burned person, may lead to death owing to the absence of a barrier against infection by external microbial organisms, as well as loss of body temperature and body fluids.

Skin tissue is composed of several layers. The outermost layer is the epidermis which is supported by a basement membrane and overlies the dermis. Beneath the dermis is loose connective tissue and fascia which cover muscles or bony tissue. The skin is a self-renewing tissue in that cells are constantly being formed and shed. The deepest cells of the epidermis are the basal cells, which are enriched in cells capable of replication. Such replicating cells are called progenitor or stem cells. Replicating cells in turn give rise to daughter cells called 'transit amplifying cells'. These cells undergo differentiation and maturation into keratinocytes (mature skin cells) as they move from the basal layer to the more superficial layers of the epidermis. In the process, keratinocytes become cornified and are ultimately shed from the skin surface. Other cells in the epidermis include melanocytes which synthesize melanin, the pigment responsible for protection against sunlight. The Langerhans cell also resides in the epidermis and functions as a cell which processes foreign proteins for presentation to the immune system.

The dermis contains nerves, blood and lymphatic vessels, fibrous and fatty tissue. Within the dermis are fibroblasts, macrophages and mast cells. Both the epidermis and dermis are penetrated by sweat, or sebaceous glands and hair follicles. Each strand of hair is derived from a hair follicle. When hair is plucked out, the hair re-grows from epithelial cells directed by the dermal papillae of the hair follicle.

When the skin surface is breached, for example in a wound, the stem cells proliferate and daughter keratinocytes migrate across the wound to reseal the tissues. The skin cells therefore possess genes activated in response to trauma. The products of these genes include several growth factors, such as epidermal growth factor, which mediate the proliferation of skin cells. The genes that are activated in the skin, and the protein products of such genes, may be developed as agents for the treatment of skin wounds. Additional growth factors derived from skin cells may also influence growth of other cell types. As skin cancers are a disorder of the growth of skin cells, proteins derived from skin that regulate cellular growth may be developed as agents for the treatment of skin cancers. Skin derived proteins that regulate the production of melanin may be useful as agents, which protect skin against unwanted effects of sunlight.

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Keratinocytes are known to secrete cytokines and express various cell surface proteins. Cytokines and cell surface molecules are proteins, which play an important role in the inflammatory response against infection, and also in autoimmune diseases affecting the skin. Genes and their protein products that are expressed by skin cells may thus be developed into agents for the treatment of inflammatory disorders affecting the skin.

Hair is an important part of a person's individuality. Disorders of the skin may lead to hair loss. Alopecia areata is a disease characterized by the patchy loss of hair over the scalp. Total baldness is a side effect of drug treatment for cancer. The growth and development of hair is mediated by the effects of genes expressed in skin and dermal papillae. Such genes and their protein products may be usefully developed into agents for the treatment of disorders of the hair follicle.

New treatments are required to hasten the healing of skin wounds, to prevent the loss of hair, enhance the re-growth of hair or removal of hair, and to treat autoimmune

and inflammatory skin diseases more effectively and without adverse effects. More effective treatments of skin cancers are also required. There thus remains a need in the art for the identification and isolation of genes encoding proteins expressed in the skin, for use in the development of therapeutic agents for the treatment of disorders including those associated with skin.

Summary of the Invention

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The present invention provides polypeptides and functional portions of polypeptides, which may be expressed in skin cells, together with polynucleotides encoding such polypeptides or functional portions thereof, expression vectors and host cells comprising such polynucleotides, and methods for their use.

In specific embodiments, isolated polynucleotides are provided that comprise a polynucleotide selected from the group consisting of: (a) sequences recited in SEQ ID NOS: 1-119, 198-276, 349-372, 399-405, 410-412, 416, 418-455, 464, 466-487, 510, 511 and 514-623; (b) complements of the sequences recited in SEQ ID NOS: 1-119, 198-276, 349-372, 399-405, 410-412, 416, 418-455, 464, 466-487, 510, 511 and 514-623; (c) reverse complements of the sequences recited in SEQ ID NOS: 1-119, 198-276, 349-372, 399-405, 410-412, 416, 418-455, 464, 466-487, 510, 511 and 514-623; (d) reverse sequences of the sequences recited in SEQ ID NOS: 1-119, 198-276, 349-372, 399-405, 410-412, 416, 418-455, 464, 466-487, 510, 511 and 514-623; (e) sequences having a 99% probability of being the same as a sequence of (a)-(d); and (f) sequences having at least 50%, 75%, 90% or 95% identity to a sequence of (a)-(d).

In further embodiments, the present invention provides isolated polypeptides comprising an amino acid sequence selected from the group consisting of: (a) sequences provided in SEQ ID NOS: 120-197, 275-348, 373-398, 406-409, 413-415, 417, 456-463, 465, 488-509, 512, 513 and 624-725; and (b) sequences having at least 50%, 75%, 90% or 95% identity to a sequence provided in SEQ ID NOS: 120-197, 275-348, 373-398, 406-409, 413-415, 417, 456-463, 465, 488-509, 512, 513 and 624-725, together with isolated polynucleotides encoding such polypeptides. Isolated polypeptides which

comprise at least a functional portion of a polypeptide comprising an amino acid sequence selected from the group consisting of: (a) sequences provided in SEQ ID NOS: 120-197, 275-348, 373-398, 406-409, 413-415, 417, 456-463, 465, 488-509, 512, 513 and 624-725; and (b) sequences having 50%, 75% or 90% identity to a sequence of SEQ ID NOS: 120-197, 275-348, 373-398, 406-409, 413-415, 417, 456-463, 465, 488-509, 512, 513 and 624-725, are also provided.

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In related embodiments, the present invention provides expression vectors comprising the above polynucleotides, together with host cells transformed with such vectors.

In a further aspect, the present invention provides a method of stimulating keratinocyte growth and motility, inhibiting the growth of epithelial-derived cancer cells, inhibiting angiogenesis and vascularization of tumors, or modulating the growth of blood vessels in a subject, comprising administering to the subject a composition comprising an isolated polypeptide, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (a) sequences provided in SEQ ID NOS: 187, 196, 342, 343, 395, 397 and 398; and (b) sequences having at least 50%, 75%, 90% or 95% identity to a sequence provided in SEQ ID NOS: 187, 196, 342, 343, 395, 397 and 398.

Methods for modulating skin inflammation in a subject are also provided, the methods comprising administering to the subject a composition comprising an isolated polypeptide, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (a) sequences provided in SEQ ID NOS: 338 and 347; and (b) sequences having at least 50%, 75%, 90% or 95% identity to a sequence provided in SEQ ID NOS: 338 and 347. In an additional aspect, the present invention provides methods for stimulating the growth of epithelial cells in a subject. Such methods comprise administering to the subject a composition comprising an isolated polypeptide including an amino acid sequence selected from the group consisting of: (a) sequences provided in SEQ ID NOS: 129 and 348; and (b) sequences having at least 50%, 75%, 90% or 95% identity to a sequence provided in SEQ ID NOS: 129 and 348.

In yet a further aspect, methods for inhibiting the binding of HIV-1 to leukocytes, for the treatment of an inflammatory disease or for the treatment of cancer in a subject are provided, the methods comprising administering to the subject a composition comprising an isolated polypeptide including an amino acid sequence selected from the group consisting of: (a) sequences provided in SEQ ID NOS: 340, 344, 345 and 346; and (b) sequences having at least 50%, 75%, 90% or 95% identity to a sequence provided in SEQ ID NOS: 340, 344, 345 and 346.

As detailed below, the isolated polynucleotides and polypeptides of the present invention may be usefully employed in the preparation of therapeutic agents for the treatment of skin disorders.

The above-mentioned and additional features of the present invention, together with the manner of obtaining them, will be best understood by reference to the following more detailed description. All references disclosed herein are incorporated herein by reference in their entirety as if each was incorporated individually.

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Brief Description of the Drawings

Fig. 1 shows the results of a Northern analysis of the distribution of huTR1 mRNA in human tissues. Key: He, Heart; Br, Brain; Pl, Placenta; Lu, Lung; Li, Liver; SM, Skeletal muscle; Ki, Kidney; Sp, Spleen; Th, Thymus; Pr, Prostate; Ov, Ovary.

Fig. 2 shows the results of a MAP kinase assay of muTR1a and huTR1a. MuTR1a (500ng/ml), huTR1a (100ng/ml) or LPS (3pg/ml) were added as described in the text.

Fig. 3 shows the stimulation of growth of neonatal foreskin keratinocytes by muTR1a.

Fig. 4 shows the stimulation of growth of the transformed human keratinocyte cell line HaCaT by muTR1a and huTR1a.

Fig. 5 shows the inhibition of growth of the human epidermal carcinoma cell line A431 by muTR1a and huTR1a.

Fig. 6 shows the inhibition of IL-2 induced growth of concanavalin A-stimulated

murine splenocytes by KS2a.

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Fig. 7 shows the stimulation of growth of rat intestinal epithelial cells (IEC-18) by a combination of KS3a plus apo-transferrin.

Fig. 8 illustrates the oxidative burst effect of TR-1 (100 ng/ml), muKS1 (100 ng/ml), SDF1 α (100 ng/ml), and fMLP (10 μ M) on human PBMC.

Figure 9 shows the chemotactic effect of muKS1 and SDF-1α on THP-1 cells.

Figure 10 shows the induction of cellular infiltrate in C3H/HeJ mice after intraperitoneal injections with muKS1 (50 μ g), GV14B (50 μ g) and PBS.

Figure 11 demonstrates the induction of phosphorylation of ERK1 and ERK2 in CV1/EBNA and HeLa cell lines by huTR1a.

Figure 12 shows the huTR1 mRNA expression in HeLa cells after stimulation by muTR1, huTR1, huTGFα and PBS (100 ng/ml each).

Figure 13 shows activation of the SRE by muTR1a in PC-12 (Fig. 13A) and HaCaT (Fig. 13B) cells.

Figure 14 shows the inhibition of huTR1a mediated growth on HaCaT cells by an antibody to the EGF receptor.

Figure 15A shows the nucleotide sequence of KS1 cDNA (SEQ ID NO: 464) along with the deduced amino acid sequence (SEQ ID NO: 465) using single letter code. The 5' UTR is indicated by negative numbers. The underlined NH₂-terminal amino acids represent the predicted leader sequence and the stop codon is denoted by ***. The polyadenylation signal is marked by a double underline. Figure 15B shows a comparison of the complete open reading frame of KS1 (referred to in Fig. 15B as KLF-1) with its human homologue BRAK and with the mouse α-chemokines mCrg-2, mMig, mSDF-1, mBLC, mMIP2, mKC and mLIX. An additional five residues are present in KS1 and BRAK between cysteine 3 and cysteine 4 that have not previously been described for chemokines.

Detailed Description of the Invention

In one aspect, the present invention provides polynucleotides that were isolated from mammalian skin cells. As used herein, the term "polynucleotide" means a single or

double-stranded polymer of deoxyribonucleotide or ribonucleotide bases and includes DNA and RNA molecules, both sense and anti-sense strands. The term comprehends cDNA, genomic DNA, recombinant DNA and wholly or partially synthesized nucleic acid molecules. A polynucleotide may consist of an entire gene, or a portion thereof. A gene is a DNA sequence that codes for a functional protein or RNA molecule. Operable anti-sense polynucleotides may comprise a fragment of the corresponding polynucleotide, and the definition of "polynucleotide" therefore includes all operable anti-sense fragments. Anti-sense polynucleotides and techniques involving anti-sense polynucleotides are well known in the art and are described, for example, in Robinson-Benion et al., "Anti-sense Techniques," *Methods in Enzymol.* 254(23):363-375, 1995; and Kawasaki et al., *Artific. Organs* 20(8):836-848, 1996.

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Identification of genomic DNA and heterologous species DNAs can be accomplished by standard DNA/DNA hybridization techniques, under appropriately stringent conditions, using all or part of a cDNA sequence as a probe to screen an appropriate library. Alternatively, PCR techniques using oligonucleotide primers that are designed based on known genomic DNA, cDNA and protein sequences can be used to amplify and identify genomic and cDNA sequences. Synthetic DNAs corresponding to the identified sequences and variants may be produced by conventional synthesis methods. All the polynucleotides provided by the present invention are isolated and purified, as those terms are commonly used in the art.

In specific embodiments, the polynucleotides of the present invention comprise a sequence selected from the group consisting of sequences provided in SEQ ID NOS: 1-119, 198-274, 349-372, 399-405, 410-412, 416, 418-455, 464, 466-487, 510, 511 and 514-623, and variants of the sequences of SEQ ID NOS: 1-119, 198-274, 349-372, 399-405, 410-412, 416, 418-455, 464, 466-487, 510, 511 and 514-623. Polynucleotides that comprise complements of such sequences, reverse complements of such sequences, or reverse sequences of such sequences, together with variants of such sequences, are also provided.

The definition of the terms "complement," "reverse complement," and "reverse sequence," as used herein, is best illustrated by the following example. For the sequence 5' AGGACC 3', the complement, reverse complement, and reverse sequence are as follows:

complement 3' TCCTGG 5'
reverse complement 3' GGTCCT 5'
reverse sequence 5' CCAGGA 3'.

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As used herein, the term "complement" refers to sequences that are fully complementary to a sequence disclosed herein.

In another aspect, the present invention provides isolated polypeptides and functional portions of polypeptides encoded, or partially encoded, by the above polynucleotides. As used herein, the term "polypeptide" encompasses amino acid chains of any length, including full length proteins, wherein the amino acid residues are linked by covalent peptide bonds. The term "polypeptide encoded by a polynucleotide" as used herein, includes polypeptides encoded by a polynucleotide which comprises a partial isolated DNA sequence provided herein. In specific embodiments, the inventive polypeptides comprise an amino acid sequence selected from the group consisting of sequences provided in SEQ ID NOS: 120-197, 275-348, 373-398, 406-409, 413-415, 417, 456-463, 465, 488-509, 512, 513 and 624-725, as well as variants of such sequences.

Polypeptides of the present invention may be produced recombinantly by inserting a DNA sequence that encodes the polypeptide into an expression vector and expressing the polypeptide in an appropriate host. Any of a variety of expression vectors known to those of ordinary skill in the art may be employed. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector containing a DNA molecule that encodes a recombinant polypeptide. Suitable host cells include prokaryotes, yeast, and higher eukaryotic cells. Preferably, the host cells employed are *E. coli*, insect, yeast, or a mammalian cell line such as COS or CHO. The DNA sequences expressed in this manner may encode naturally occurring polypeptides, portions of naturally occurring polypeptides, or other variants thereof.

In a related aspect, polypeptides are provided that comprise at least a functional portion of a polypeptide having an amino acid sequence selected from the group consisting of sequences provided in SEQ ID NOS: 120-197, 275-348, 373-398, 406-409, 413-415, 417, 456-463, 465, 488-509, 512-513 and 624-725, and variants thereof. As used herein, the "functional portion" of a polypeptide is that portion which contains the active site essential for affecting the function of the polypeptide, for example, the portion of the molecule that is capable of binding one or more reactants. The active site may be made up of separate portions present on one or more polypeptide chains and will generally exhibit high binding affinity.

Functional portions of a polypeptide may be identified by first preparing fragments of the polypeptide by either chemical or enzymatic digestion of the polypeptide, or by mutation analysis of the polynucleotide that encodes the polypeptide and subsequent expression of the resulting mutant polypeptides. The polypeptide fragments or mutant polypeptides are then tested to determine which portions retain biological activity, using, for example, the representative assays provided below.

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Portions and other variants of the inventive polypeptides may also be generated by synthetic or recombinant means. Synthetic polypeptides having fewer than about 100 amino acids, and generally fewer than about 50 amino acids, may be generated using techniques well known to those of ordinary skill in the art. For example, such polypeptides may be synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain. See Merrifield, J. Ani. Chem. Soc. 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems, Inc. (Foster City, California), and may be operated according to the manufacturer's instructions. Variants of a native polypeptide may be prepared using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis (Kunkel, T., Proc. Natl. Acad. Sci. USA 82:488-492, 1985). Sections of DNA sequence

may also be removed using standard techniques to permit preparation of truncated polypeptides.

In general, the polypeptides disclosed herein are prepared in an isolated, substantially pure, form. Preferably, the polypeptides are at least about 80% pure, more preferably at least about 90% pure, and most preferably at least about 99% pure. In certain preferred embodiments, described in detail below, the isolated polypeptides are incorporated into pharmaceutical compositions or vaccines for use in the treatment of skin disorders.

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As used herein, the term "variant" comprehends nucleotide or amino acid sequences different from the specifically identified sequences, wherein one or more nucleotides or amino acid residues is deleted, substituted, or added. Variants may be naturally occurring allelic variants, or non-naturally occurring variants. In certain preferred embodiments, variants of the inventive sequences retain certain, or all, of the functional characteristics of the inventive sequence. Variant sequences (polynucleotide or polypeptide) preferably exhibit at least 50%, more preferably at least 75%, and most preferably at least 90% or 95% identity to a sequence of the present invention. The percentage identity is determined by aligning the two sequences to be compared as described below, determining the number of identical residues in the aligned portion, dividing that number by the total number of residues in the inventive (queried) sequence, and multiplying the result by 100.

Polynucleotide or polypeptide sequences may be aligned, and percentages of identical nucleotides in a specified region may be determined against another polynucleotide or polypeptide, using computer algorithms that are publicly available. Two exemplary algorithms for aligning and identifying the similarity of polynucleotide sequences are the BLASTN and FASTA algorithms. The alignment and similarity of polypeptide sequences may be examined using the BLASTP and algorithm. BLASTX and FASTX algorithms compare nucleotide query sequences translated in all reading frames against polypeptide sequences. The BLASTN, BLASTP and BLASTX algorithms are available on the NCBI anonymous FTP server (ftp://ncbi.nlm.nih.gov)

under /blast/executables/ and are available from the National Center for Biotechnology Information (NCBI), National Library of Medicine, Building 38A, Room 8N805, Bethesda, MD 20894 USA.

The FASTA and FASTX algorithms are available on the Internet at the ftp site ftp://ftp.Virginia.edu/pub/. The FASTA software package is also available from the University of Virginia by contacting David Hudson, Assistant Provost for Research, University of Virginia, PO Box 9025, Charlottesville, VA 22906-9025. The FASTA algorithm, set to the default parameters described in the documentation and distributed with the algorithm, may be used in the determination of polynucleotide variants. The readme files for FASTA and FASTX v1.0x that are distributed with the algorithms describe the use of the algorithms and describe the default parameters. The use of the FASTA and FASTX algorithms is also described in Pearson, and Lipman, *Proc. Natl. Acad. Sci. USA* 85:2444-2448, 1988; and Pearson, *Methods in Enzymol.* 183:63-98, 1990.

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The BLASTN algorithm version 2.0.4 [Feb-24-1998], 2.0.6 [Sept-16-1998] and 2.0.11 [Jan-20-2000], set to the default parameters described in the documentation and distributed with the algorithm, is preferred for use in the determination of polynucleotide variants according to the present invention. The BLASTP algorithm version 2.0.4, 2.0.6 and 2.0.11, set to the default parameters described in the documentation and distributed with the algorithm, is preferred for use in the determination of polypeptide variants according to the present invention. The use of the BLAST family of algorithms, including BLASTN, BLASTP and BLASTX is described in the publication of Altschul, et al., Nucleic Acids Res. 25:3389-3402, 1997.

The following running parameters are preferred for determination of alignments and similarities using BLASTN that contribute to the E values and percentage identity for polynucleotides: Unix running command with default parameters thus: blastall -p blastn - d embldb -e 10 -G 0 -E 0 -r 1 -v 30 -b 30 -i queryseq -o results; and parameters are: -p Program Name [String]; -d Database [String]; -e Expectation value (E) [Real]; -G Cost to open a gap (zero invokes default behavior) [Integer]; -E Cost to extend a gap (zero

invokes default behavior) [Integer]; -r Reward for a nucleotide match (blastn only) [Integer]; -v Number of one-line descriptions (V) [Integer]; -b Number of alignments to show (B) [Integer]; -i Query File [File In]; -o BLAST report Output File [File Out] Optional. The following running parameters are preferred for determination of alignments and similarities using BLASTP that contribute to the E values and percentage identity for polypeptides: blastall -p blastp -d swissprotdb -e 10 -G 1 -E 11 -r 1 -v 30 -b 30 -i queryseq -o results; and the parameters are: -p Program Name [String]; -d Database [String]; -e Expectation value (E) [Real]; -G Cost to open a gap (zero invokes default behavior) [Integer]; -E Cost to extend a gap (zero invokes default behavior) [Integer]; -v Number of one-line descriptions (v) [Integer]; -b Number of alignments to show (b) [Integer]; -I Query File [File In]; -o BLAST report Output File [File Out] Optional.

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The "hits" to one or more database sequences by a queried sequence produced by BLASTN, BLASTP, FASTA, or a similar algorithm, align and identify similar portions of sequences. The hits are arranged in order of the degree of similarity and the length of sequence overlap. Hits to a database sequence generally represent an overlap over only a fraction of the sequence length of the queried sequence.

As noted above, the percentage identity of a polynucleotide or polypeptide sequence is determined by aligning polynucleotide and polypeptide sequences using appropriate algorithms, such as BLASTN or BLASTP, respectively, set to default parameters; identifying the number of identical nucleic or amino acids over the aligned portions; dividing the number of identical nucleic or amino acids by the total number of nucleic or amino acids of the polynucleotide or polypeptide of the present invention; and then multiplying by 100 to determine the percentage identity. By way of example, a queried polynucleotide having 220 nucleic acids has a hit to a polynucleotide sequence in the EMBL database having 520 nucleic acids over a stretch of 23 nucleotides in the alignment produced by the BLASTN algorithm using the default parameters. The 23 nucleotide hit includes 21 identical nucleotides, one gap and one different nucleotide. The percentage identity of the queried polynucleotide to the hit in the EMBL database is

thus 21/220 times 100, or 9.5%. The identity of polypeptide sequences may be determined in a similar fashion.

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The BLASTN and BLASTX algorithms also produce "Expect" values for polynucleotide and polypeptide alignments. The Expect value (E) indicates the number of hits one can "expect" to see over a certain number of contiguous sequences by chance when searching a database of a certain size. The Expect value is used as a significance threshold for determining whether the hit to a database indicates true similarity. For example, an E value of 0.1 assigned to a polynucleotide hit is interpreted as meaning that in a database of the size of the EMBL database, one might expect to see 0.1 matches over the aligned portion of the sequence with a similar score simply by chance. By this criterion, the aligned and matched portions of the sequences then have a probability of 90% of being the same. For sequences having an E value of 0.01 or less over aligned and matched portions, the probability of finding a match by chance in the EMBL database is 1% or less using the BLASTN algorithm. E values for polypeptide sequences may be determined in a similar fashion using various polypeptide databases, such as the SwissProt database.

According to one embodiment, "variant" polynucleotides and polypeptides, with reference to each of the polynucleotides and polypeptides of the present invention, preferably comprise sequences having the same number or fewer nucleic or amino acids than each of the polynucleotides or polypeptides of the present invention and producing an E value of 0.01 or less when compared to the polynucleotide or polypeptide of the present invention. That is, a variant polynucleotide or polypeptide is any sequence that has at least a 99% probability of being the same as the polynucleotide or polypeptide of the present invention, measured as having an E value of 0.01 or less using the BLASTN or BLASTX algorithms set at the default parameters. According to a preferred embodiment, a variant polynucleotide is a sequence having the same number or fewer nucleic acids than a polynucleotide of the present invention that has at least a 99% probability of being the same as the polynucleotide of the present invention, measured as having an E value of 0.01 or less using the BLASTN algorithm set at the default

parameters. Similarly, according to a preferred embodiment, a variant polypeptide is a sequence having the same number or fewer amino acids than a polypeptide of the present invention that has at least a 99% probability of being the same as the polypeptide of the present invention, measured as having an E value of 0.01 or less using the BLASTP algorithm set at the default parameters.

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Variant polynucleotide sequences will generally hybridize to the recited polynucleotide sequences under stringent conditions. As used herein, "stringent conditions" refers to prewashing in a solution of 6X SSC, 0.2% SDS; hybridizing at 65°C, 6X SSC, 0.2% SDS overnight; followed by two washes of 30 minutes each in 1X SSC, 0.1% SDS at 65 °C and two washes of 30 minutes each in 0.2X SSC, 0.1% SDS at 65 °C.

As used herein, the term "x-mer," with reference to a specific value of "x," refers to a polynucleotide or polypeptide, respectively, comprising at least a specified number ("x") of contiguous residues of: any of the polynucleotides provided in SEQ ID NO: 1-119, 198-274, 349-372, 399-405, 410-412, 416, 418-455, 464, 466-487, 510, 511 and 514-623; or any of the polypeptides set out in SEQ ID NO: 120-197, 275-348, 373-398, 406-409, 413-415, 417, 456-463, 465, 488-509, 512, 513 and 624-725. The value of x may be from about 20 to about 600, depending upon the specific sequence.

Polynucleotides of the present invention comprehend polynucleotides comprising at least a specified number of contiguous residues (*x*-mers) of any of the polynucleotides identified as SEQ ID NO: 1-119, 198-274, 349-372, 399-405, 410-412, 416, 418-455, 464, 466-487, 510, 511 and 514-623, or their variants. Polypeptides of the present invention comprehend polypeptides comprising at least a specified number of contiguous residues (*x*-mers) of any of the polypeptides identified as SEQ ID NO: 120-197, 275-348, 373-398, 406-409, 413-415, 417, 456-463, 465, 488-509, 512, 513 and 624-725. According to preferred embodiments, the value of *x* is at least 20, more preferably at least 40, more preferably yet at least 60, and most preferably at least 80. Thus, polynucleotides of the present invention include polynucleotides comprising a 20-mer, a 40-mer, a 60-mer, an 80-mer, a 100-mer, a 120-mer, a 150-mer, a 180-mer, a 220-mer, a

250-mer; or a 300-mer, 400-mer, 500-mer or 600-mer of a polynucleotide provided in SEQ ID NOS: 1-119, 198-274, 349-372, 399-405, 410-412, 416, 418-455, 464, 466-487, 510, 511 and 514-623, or of a variant of one of the polynucleotides provided in SEQ ID NO: 1-119, 198-274, 349-372, 399-405, 410-412, 416, 418-455, 464, 466-487, 510, 511 and 514-623. Polypeptides of the present invention include polypeptides comprising a 20-mer, a 40-mer, a 60-mer, an 80-mer, a 100-mer, a 120-mer, a 150-mer, a 180-mer, a 220-mer, a 250-mer; or a 300-mer, 400-mer, 500-mer or 600-mer of a polypeptide provided in SEQ ID NOS: 120-197, 275-348, 373-398, 406-409, 413-415, 417, 456-463, 465, 488-509, 512, 513 and 624-725, or of a variant of one of the polypeptides provided in SEQ ID NOS: 120-197, 275-348, 373-398, 406-409, 413-415, 417, 456-463, 465, 488-509, 512, 513 and 624-725.

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The inventive polynucleotides may be isolated by high throughput sequencing of cDNA libraries prepared from mammalian skin cells as described below in Example 1. Alternatively, oligonucleotide probes based on the sequences provided in SEQ ID NOS: 1-119, 198-274, 349-372, 399-405, 410-412, 416, 418-455, 464, 466-487, 510, 511 and 514-623 can be synthesized and used to identify positive clones in either cDNA or genomic DNA libraries from mammalian skin cells by means of hybridization or polymerase chain reaction (PCR) techniques. Probes can be shorter than the sequences provided herein but should be at least about 10, preferably at least about 15 and most preferably at least about 20 nucleotides in length. Hybridization and PCR techniques suitable for use with such oligonucleotide probes are well known in the art (see, for example, Mullis, et al., Cold Spring Harbor Symp. Quant. Biol., 51:263, 1987; Erlich, ed., PCR Technology, Stockton Press: NY, 1989; (Sambrook, J, Fritsch, EF and Maniatis, T, eds., Molecular Cloning: A Laboratory Manual, 2nd ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor: New York, 1989). Positive clones may be analyzed by restriction enzyme digestion, DNA sequencing or the like.

In addition, DNA sequences of the present invention may be generated by synthetic means using techniques well known in the art. Equipment for automated synthesis of oligonucleotides is commercially available from suppliers such as Perkin

Elmer/Applied Biosystems Division (Foster City, California) and may be operated according to the manufacturer's instructions.

Since the polynucleotide sequences of the present invention have been derived from skin, they likely encode proteins that have important roles in growth and development of skin, and in responses of skin to tissue injury and inflammation as well as disease states. Some of the polynucleotides contain sequences that code for signal sequences, or transmembrane domains, which identify the protein products as secreted molecules or receptors. Such protein products are likely to be growth factors, cytokines, or their cognate receptors. Several of the polypeptide sequences have more than 25% similarity to known biologically important proteins and thus are likely to represent proteins having similar biological functions.

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In particular, the inventive polypeptides have important roles in processes such as: induction of hair growth; differentiation of skin stem cells into specialized cell types; cell migration; cell proliferation and cell-cell interaction. The polypeptides are important in the maintenance of tissue integrity, and thus are important in processes such as wound healing. Some of the disclosed polypeptides act as modulators of immune responses, especially since immune cells are known to infiltrate skin during tissue insult causing growth and differentiation of skin cells. In addition, many polypeptides are immunologically active, making them important therapeutic targets in a whole range of disease states not only within skin, but also in other tissues of the body. Antibodies to the polypeptides of the present invention and small molecule inhibitors related to the polypeptides of the present invention may also be used for modulating immune responses and for treatment of diseases according to the present invention.

In one aspect, the present invention provides methods for using one or more of the inventive polypeptides or polynucleotides to treat disorders in a patient. As used herein, a "patient" refers to any warm-blooded animal, preferably a human.

In this aspect, the polypeptide or polynucleotide is generally present within a pharmaceutical or immunogenic composition. Pharmaceutical compositions may comprise one or more polypeptides, each of which may contain one or more of the above

sequences (or variants thereof), and a physiologically acceptable carrier. Immunogenic compositions may comprise one or more of the above polypeptides and a non-specific immune response amplifier, such as an adjuvant or a liposome, into which the polypeptide is incorporated.

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Alternatively, a pharmaceutical or immunogenic composition of the present invention may contain DNA encoding one or more polypeptides as described above, such that the polypeptide is generated in situ. In such compositions, the DNA may be present within any of a variety of delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, and bacterial and viral expression systems. Appropriate nucleic acid expression systems contain the necessary DNA sequences for expression in the patient (such as a suitable promoter and terminator signal). Bacterial delivery systems involve the administration of a bacterium (such as Bacillus-Calmette-Guerin) that expresses an immunogenic portion of the polypeptide on its cell surface. In a preferred embodiment, the DNA may be introduced using a viral expression system (e.g., vaccinia or other poxvirus, retrovirus, or adenovirus), which may involve the use of a non-pathogenic, or defective, replication competent virus. Techniques for incorporating DNA into such expression systems are well known in the art. The DNA may also be "naked," as described, for example, in Ulmer et al., Science 259:1745-1749, 1993 and reviewed by Cohen, Science 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported into the cells.

Routes and frequency of administration, as well as dosage, vary from individual to individual. In general, the pharmaceutical and immunogenic compositions may be administered by injection (e.g., intradermal, intramuscular, intravenous, or subcutaneous), intranasally (e.g., by aspiration) or orally. In general, the amount of polypeptide present in a dose (or produced *in situ* by the DNA in a dose) ranges from about 1 pg to about 100 mg per kg of host, typically from about 10 pg to about 1 mg per kg of host, and preferably from about 100 pg to about 1 µg per kg of host. Suitable dose

sizes will vary with the size of the patient, but will typically range from about 0.1 ml to about 5 ml.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will vary depending on the mode of administration. For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a lipid, a wax, or a buffer. For oral administration, any of the above carriers or a solid carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and magnesium carbonate, may be employed. Biodegradable microspheres (e.g., polylactic galactide) may also be employed as carriers for the pharmaceutical compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S. Patent Nos. 4,897,268 and 5,075,109.

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Any of a variety of adjuvants may be employed in the immunogenic compositions of the invention to non-specifically enhance the immune response. Most adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a non-specific stimulator of immune responses, such as lipid A, *Bordetella pertussis*, or *Mycobacterium tuberculosis*. Suitable adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Freund's Complete Adjuvant (Difco Laboratories, Detroit, Michigan), and Merck Adjuvant 65 (Merck and Company, Inc., Rahway, New Jersey). Other suitable adjuvants include alum, biodegradable microspheres, monophosphoryl lipid A, and Quil A.

The polynucleotides of the present invention may also be used as markers for tissue, as chromosome markers or tags, in the identification of genetic disorders, and for the design of oligonucleotides for examination of expression patterns using techniques well known in the art, such as the microarray technology available from Affymetrix (Santa Clara, CA). Partial polynucleotide sequences disclosed herein may be employed to obtain full length genes by, for example, screening of DNA expression libraries using hybridization probes or PCR primers based on the inventive sequences.

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The polypeptides provided by the present invention may additionally be used in assays to determine biological activity, to raise antibodies, to isolate corresponding ligands or receptors, in assays to quantitatively determine levels of protein or cognate corresponding ligand or receptor, as anti-inflammatory agents, and in compositions for skin, connective tissue and/or nerve tissue growth or regeneration. The present invention further provides methods for modulating expression of the inventive polypeptides, for example by inhibiting translation of the relevant polynucleotide. Translation of the relevant polynucleotide may be inhibited, for example, by introducing anti-sense expression vectors; by introducing antisense oligodeoxyribonucleotides or antisense phosphorothioate oligodeoxyribonucleotides; by introducing antisense oligoribonucleotides or antisense phosphorothioate oligoribonucleotides; or by other means which are well known in the art. Cell permeation and activity of antisense oligonucleotides can be enhanced by appropriate chemical modifications, such as the use of phenoxazine-substituted C-5 propynyl uracil oligonucleotides (Flanagan et al., (1999) Nat. Biotechnol. 17 (1): 48-52) or 2'-O-(2-methoxy) ethyl (2'-MOE)-oligonucleotides (Zhang et al., (2000) Nat. Biotechnol. 18: 862-867). The use of techniques involving antisense polynucleotides is well known in the art and is described, for example, in Robinson-Benion et al. (1995), Antisense techniques, Methods in Enzymol. 254 (23): 363-375 and Kawasaki et al. (1996), Artific. Organs 20 (8): 836-848.

The following Examples are offered by way of illustration and not by way of limitation.

Example 1

ISOLATION OF CDNA SEQUENCES FROM SKIN CELL EXPRESSION LIBRARIES

The cDNA sequences of the present invention were obtained by high-throughput sequencing of cDNA expression libraries constructed from specialized rodent or human skin cells as shown in Table 1.

	<u>Table 1</u>	
Library	Skin cell type	Source
DEPA	dermal papilla	rat

SKTC	keratinocytes	human
HNFF	neonatal foreskin fibroblast	human
MEMS	embryonic skin	mouse
KSČL	keratinocyte stem cell	mouse
TRAM	transit amplifying cells	mouse
MFSE	epidermis	mouse
HLEA	small epithelial airway cells	human
HLEB	small epithelial airway cells	human
HNKA	NK cells	human

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These cDNA libraries were prepared as described below.

cDNA Library from Dermal Papilla (DEPA)

Dermal papilla cells from rat hair vibrissae (whiskers) were grown in culture and the total RNA extracted from these cells using established protocols. Total RNA, isolated using TRIzol Reagent (BRL Life Technologies, Gaithersburg, Maryland), was used to obtain mRNA using a Poly(A) Quik mRNA isolation kit (Stratagene, La Jolla, California), according to the manufacturer's specifications. A cDNA expression library was then prepared from the mRNA by reverse transcriptase synthesis using a Lambda ZAP cDNA library synthesis kit (Stratagene).

cDNA Library from Keratinocytes (SKTC)

Keratinocytes obtained from human neonatal foreskins (Mitra, R and Nikoloff, B in *Handbook of Keratinocyte Methods*, pp. 17-24, 1994) were grown in serum-free KSFM (BRL Life Technologies) and harvested along with differentiated cells (10⁸ cells). Keratinocytes were allowed to differentiate by addition of fetal calf serum at a final concentration of 10% to the culture medium and cells were harvested after 48 hours. Total RNA was isolated from the two cell populations using TRIzol Reagent (BRL Life Technologies) and used to obtain mRNA using a Poly(A) Quik mRNA isolation kit

(Stratagene). cDNAs expressed in differentiated keratinocytes were enriched by using a PCR-Select cDNA Subtraction Kit (Clontech, Palo Alto, California). Briefly, mRNA was obtained from either undifferentiated keratinocytes ("driver mRNA") or differentiated keratinocytes ("tester mRNA") and used to synthesize cDNA. The two populations of cDNA were separately digested with *RsaI* to obtain shorter, blunt-ended molecules. Two tester populations were created by ligating different adaptors at the cDNA ends and two successive rounds of hybridization were performed with an excess of driver cDNA. The adaptors allowed for PCR amplification of only the differentially expressed sequences which were then ligated into T-tailed pBluescript (Hadjeb, N and Berkowitz, GA, *BioTechniques* 20:20-22 1996), allowing for a blue/white selection of cells containing vector with inserts. White cells were isolated and used to obtain plasmid DNA for sequencing.

cDNA library from human neonatal fibroblasts (HNFF)

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Human neonatal fibroblast cells were grown in culture from explants of human neonatal foreskin and the total RNA extracted from these cells using established protocols. Total RNA, isolated using TRIzol Reagent (BRL Life Technologies, Gaithersburg, Maryland), was used to obtain mRNA using a Poly(A) Quik mRNA isolation kit (Stratagene, La Jolla, California), according to the manufacturer's specifications. A cDNA expression library was then prepared from the mRNA by reverse transcriptase synthesis using a Lambda ZAP cDNA library synthesis kit (Stratagene).

cDNA library from mouse embryonic skin (MEMS)

Embryonic skin was micro-dissected from day 13 post coitum Balb/c mice. Embryonic skin was washed in phosphate buffered saline and mRNA directly isolated from the tissue using the Quick Prep Micro mRNA purification kit (Pharmacia, Sweden). The mRNA was then used to prepare cDNA libraries as described above for the DEPA library.

30 <u>cDNA library from mouse stem cells (KSCL)</u> and transit amplifying (TRAM) cells

Pelts obtained from 1-2 day post-partum neonatal Balb/c mice were washed and incubated in trypsin (BRL Life Technologies) to separate the epidermis from the dermis. Epidermal tissue was disrupted to disperse cells, which were then resuspended in growth medium and centrifuged over Percoll density gradients prepared according to the manufacturer's protocol (Pharmacia, Sweden). Pelleted cells were labeled using Rhodamine 123 (Bertoncello I, Hodgson GS and Bradley TR, Exp Hematol. 13:999-1006, 1985), and analyzed by flow cytometry (Epics Elite Coulter Cytometry, Hialeah, Florida). Single cell suspensions of rhodamine-labeled murine keratinocytes were then labeled with a cross reactive anti-rat CD29 biotin monoclonal antibody (Pharmingen, San Diego, California; clone Ha2/5). Cells were washed and incubated with anti-mouse CD45 phycoerythrin conjugated monoclonal antibody (Pharmingen; clone 30F11.1, 10ug/ml) followed by labeling with streptavidin spectral red (Southern Biotechnology, Birmingham, Alabama). Sort gates were defined using listmode data to identify four populations: CD29 bright rhodamine dull CD45 negative cells; CD29 bright rhodamine bright CD45 negative cells; CD29 dull rhodamine bright CD45 negative cells; and CD29 dull rhodamine dull CD45 negative cells. Cells were sorted, pelleted and snap frozen prior to storage at -80°C. This protocol was followed multiple times to obtain sufficient cell numbers of each population to prepare cDNA libraries. Skin stem cells and transit amplifying cells are known to express CD29, the integrin β1 chain. CD45, a leukocyte specific antigen, was used as a marker for cells to be excluded in the isolation of skin stem cells and transit amplifying cells. Keratinocyte stem cells expel the rhodamine dye more efficiently than transit amplifying cells. The CD29 bright, rhodamine dull, CD45 negative population (putative keratinocyte stem cells; referred to as KSCL), and the CD29 bright, rhodamine bright, CD45 negative population (keratinocyte transit amplifying cells; referred to as TRAM) were sorted and mRNA was directly isolated from each cell population using the Quick Prep Micro mRNA purification kit (Pharmacia, Sweden). The mRNA was then used to prepare cDNA libraries as described above for the DEPA library.

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cDNA Library from Epithelial Cells (MFSE)

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Skin epidermis was removed from flaky skin fsn -/- mice (The Jackson Laboratory, Bar Harbour, ME), the cells dissociated and the resulting single cell suspension placed in culture. After four passages, the cells were harvested. Total RNA, isolated using TRIzol Reagent (BRL Life Technologies, Gaithersburg, MD), was used to obtain mRNA using a Poly(A)Quik mRNA isolation kit (Stratagene, La Jolla, CA), according to the manufacturer's specifications. A cDNA expression library (referred to as the MFSE library) was then prepared from the mRNA by Reverse Transcriptase synthesis using a Lambda ZAP Express cDNA library synthesis kit (Stratagene, La Jolla, CA).

cDNA Libraries from Human Small Airway Epithelial Cells (HLEA and HLEB)

Human small airway epithelium cells SAEC (Cell line number CC-2547, Clonetics Normal Human Cell Systems, Cambrex Corporation, East Rutherford NJ) transformed with human papilloma virus E6E7 that was infected with the bacterium $Yersinia\ enterocolitica\ (ATCC\ No.\ 51871,\ American\ Type\ Culture\ Collection,\ Manassas\ VA)$ and the long form of the Respiratory Syncytial Virus (RSV, ATCC No. VR26), were used as source of RNA to construct the libraries called HLEA and HLEB. Cells from the twelfth passage of SAEC cells were infected with Y. enterocolitica for 2 hours at an initial seed of 12.5 bacteria per cell. The cells were disinfected with gentamycin (100 μ g/ml) for 2 hours and harvested 4 hours after infection. The cells were then infected with RSV at a moiety of infection of 0.7 for 1 hour and incubated for 6 and 24 hours. Cells were harvested and the RNA extracted following standard protocols.

Total RNA, isolated using TRIzol Reagent (BRL Life Technologies, Gaithersburg, Maryland), was used to obtain mRNA using a Poly(A) Quik mRNA isolation kit (Stratagene, La Jolla, CA), according to the manufacturer's specifications. Two cDNA expression libraries were then prepared from the mRNA by reverse transcriptase synthesis using a Lambda ZAP cDNA library synthesis kit (Stratagene).

cDNA Library from Epithelial Cells (HNKA)

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The subtracted cDNA library (HNKA) from human natural killer (NK) cells was constructed as follows. A NK library was first constructed using pooled RNA extracted from primary NK cells from multiple donors, stimulated for 4 or 20 hours with IL-2 (10 ng/ml), IL-12 (1 ng/ml), IL-15 (50 ng/ml), interferon alpha (IFN-α; 1,000 U/ml) immobilized anti-CD16 or immobilized anti-NAIL antibody, or from unstimulated cells. RNA was extracted following standard procedures. cDNA was prepared using a TimeSaver kit (Pharmacia, Uppsala, Sweden) following the manufacturer's protocol. The cDNA was ligated to *Bgl*II adaptors and size-selected using cDNA sizing columns (Gibco BRL, Gaithersburg MD). The size-selected NK cDNA was ligated into a pDc 409 vector and transformed into *E. coli* DH105 cells. Single-stranded DNA was prepared from the plasmid library using a helper phage (Stratagene)

A second cDNA library (referred to as FF cDNA library) was constructed using fetal foreskin tissue. RNA was extracted and cDNA prepared following standard protocols. The cDNA was ligated into the plasmid pBluescript following standard protocols. $10~\mu g$ of the FF cDNA library was linearized with the restriction endonuclease *Not*I and used as template to synthesize biotin-labeled cRNA using SP6 polymerase.

The subtracted NK cell library (HNKA) was constructed as follows. The biotinylated FF cRNA was mixed with the NK library, ethanol precipitated and resuspended in $5 \,\mu$ l buffer (50 mM HEPES pH 7.4, 10 mM EDTA, 1.5 M NaCl, 0.2% SDS). After addition of $5 \,\mu$ l formamide and heating to 95° for 1 min, the material was left to hybridize for 24 hours at 42°C. 90 μ l of 10 mM HEPES pH 7.3, 1 mM EDTA and 15 μ l streptavidin was added followed by an incubation for 20 min at 50°C. This step was repeated again after extraction with phenol/chloroform.

To the final extracted aqueous phase, the following were added: NaCl to 0.2 M, 1 μ l glycogen and 2 volumes of ethanol. After an overnight precipitation at -20°C, the DNA was pelleted and resuspended in 10 μ l water. A second round of subtraction was performed as above and the DNA transformed into *E. coli* DH105.

cDNA sequences were obtained by high-throughput sequencing of the cDNA libraries described above using a Perkin Elmer/Applied Biosystems Division Prism 377 sequencer.

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Example 2

CHARACTERIZATION OF ISOLATED CDNA SEQUENCES

The isolated cDNA sequences were compared to sequences in the EMBL DNA database using the computer algorithms FASTA and/or BLASTN. The corresponding protein sequences (DNA translated to protein in each of 6 reading frames) were compared to sequences in the SwissProt database using the computer algorithms FASTX and/or BLASTX. Comparisons of DNA sequences provided in SEQ ID NO: 1-119 to sequences in the EMBL DNA database (using FASTA) and amino acid sequences provided in SEQ ID NO: 120-197 to sequences in the SwissProt database (using FASTX) were made as of March 21, 1998. Comparisons of DNA sequences provided in SEQ ID NO: 198-274 to sequences in the EMBL DNA database (using BLASTN) and amino acid sequences provided in SEO ID NO: 275-348 to sequences in the SwissProt database (using BLASTP) were made as of October 7, 1998. Comparisons of DNA sequences provided in SEQ ID NO: 349-372 to sequences in the EMBL DNA database (using BLASTN) and amino acid sequences provided in SEQ ID NO: 373-398 to sequences in the SwissProt database (using BLASTP) were made as of January 23, 1999. Comparisons of polynucleotide sequences provided in SEQ ID NO: 418-455 and 466-487 to sequences in the EMBL DNA database (using BLASTN) and polypeptide sequences provided in SEQ ID NO: 456-463 and 488-509 to sequences in the SwissProt database (using BLASTP) were made as of April 23, 2000. Comparisons of polynucleotide sequences provided in SEQ ID NO: 510 and 511 to sequences in the EMBL DNA database (using BLASTN) and polypeptide sequences provided in SEQ ID NO: 512 and 513 to sequences in the SwissProt database (using BLASTP) were made as of July 11, 2000. Comparisons of polynucleotide sequences provided in SEQ ID NO: 514-623 to

sequences in the EMBL66 - HTGs + ENSEMBL (May 1, 2001) DNA database (using BLASTN) and polypeptide sequences provided in SEQ ID NO: 624-725 to sequences in the SP_TR_NRDB + ENSEMBL (April 30, 2001) database (using BLASTP) were made as of May 16, 2001.

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Isolated cDNA sequences and their corresponding polypeptide sequences were computer analyzed for the presence of signal sequences identifying secreted molecules. Isolated cDNA sequences that have a signal sequence at a putative start site within the sequence are provided in SEQ ID NO: 1-44, 198-238, 349-358, 399, 418-434, 440-449 and 466-471, 516, 519, 520, 523-527, 531, 532, 535-537, 548, 555, 574-580, 585-587, 589, 593, 595, 596, 598-601, 605-607, 609, 612, 613, 615, 616 and 622. The cDNA sequences of SEQ ID NO: 1-6, 198-199, 349-352, 354, 356-358,419-428, 430-433, 440-444, 446-448, 466, 468-470, 519, 520, 523, 524, 529, 531, 532, 535-537, 579, 585, 587, 598, 605, 609, 613 and 622 were determined to have less than 75% identity (determined as described above), to sequences in the EMBL database using the computer algorithms FASTA or BLASTN, as described above. The polypeptide sequences of SEQ ID NO: 120-125, 275-276, 373-380, 382, 456, 457, 460-462, 488-493, 633, 637, 642, 683, 685, 691, 693, 703, 706, 710, 714, 717, 718, 720, 721 and 725 were determined to have less than 75% identity (determined as described above) to sequences in the SwissProt database using the computer algorithms FASTX or BLASTP, as described above.

Further sequencing of some of the isolated partial cDNA sequences resulted in the isolation of the full-length cDNA sequences provided in SEQ ID NOS: 7-14, 200-231, 372, 418-422, 441-448, 514, 516, 557-561, 567, 568, 619 and 621. The polypeptide sequences encoded by the cDNA sequences of SEQ ID NO: 7-14, 200-231, 372, 514, 516, 557-561, 567, 568, 619 and 621 are provided in SEQ ID NOS: 126-133, 277-308, 396,624, 626, 666-669, 674 and 724 respectively. The cDNA sequences of SEQ ID NO: 418-422 encode the same amino acid sequences as the cDNA sequences of SEQ ID NO: 7 and 11-14, namely SEQ ID NO: 126 and 130-133, respectively. Comparison of the full-

length cDNA sequences with those in the EMBL database using the computer algorithm FASTA or BLASTN, as described above, revealed less than 75% identity (determined as described above) to known sequences, except for the polynucleotides in SEQ ID NOS: 516, 560 and 619. Comparison of the amino acid sequences provided in SEQ ID NOS: 126-133, 277-308, 666, 668, 669 and 724 with those in the SwissProt database using the computer algorithms FASTX or BLASTP, as described above, revealed less than 75% identity (determined as described above) to known sequences.

Comparison of the polypeptide sequences corresponding to the cDNA sequences of SEQ ID NOS: 15-23 with those in the EMBL database using the computer algorithm FASTA database showed less than 75% identity (determined as described above) to known sequences. These polypeptide sequences are provided in SEQ ID NOS: 134-142.

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Further sequencing of some of the isolated partial cDNA sequences resulted in the isolation of full-length cDNA sequences provided in SEQ ID NOS: 24-44, 232-238, 423-434, 449, 466, 468-470, 475, 476 and 484. The polypeptide sequences encoded by the cDNA sequences of SEQ ID NO: 24-44, 232-238, 429, 466, 468-470, 475, 476 and 484 are provided in SEQ ID NOS: 143-163, 309-315, 456, 488, 490-492, 497, 498 and 506, respectively. The cDNA sequences of SEQ ID NO: 423-428, 430-434 and 449 encode the same polypeptide sequences as the cDNA sequences of SEQ ID NO: 27-29, 34, 35, 37, 40-44 and 238, namely SEQ ID NO: 146-148, 153, 154, 156, 159-163 and 315, respectively. These polypeptide sequences were determined to have less than 75% identity, determined as described above to known sequences in the SwissProt database using the computer algorithm FASTX.

Isolated cDNA sequences having less than 75% identity to known expressed sequence tags (ESTs) or to other DNA sequences in the public database, or whose corresponding polypeptide sequence showed less than 75% identity to known protein sequences, were computer analyzed for the presence of transmembrane domains coding for putative membrane-bound molecules. Isolated cDNA sequences that have one or more transmembrane domain(s) within the sequence are provided in SEQ ID NOS: 45-63, 239-253, 359-364, 400-402, 435, 436, 450-452, 455, 470-472, 542, 553-555, 573,

576, 581, 592, 593, 595 and 606. The cDNA sequences of SEQ ID NOS: 45-48, 239-249, 359-361, 363, 450, 451, 455, 472, 473, 553-555, 573, 576 and 592 were found to have less than 75% identity (determined as described above) to sequences in the EMBL database, using the FASTA or BLASTN computer algorithms. The polypeptide sequences encoded by the cDNA sequences of SEQ ID NO: 45-48, 239-249, 359-361, 363, 450, 451, 472, 473, 553-555, 573 and 606 (provided in SEQ ID NOS: 164-167, 316-326, 383, 385-388, 407-408, 460, 461, 494, 495, 662, 663, 664, 679, 682 and 711 respectively) were found to have less than 75% identity, determined as described above, to sequences in the SwissProt database using the FASTX or BLASTP database. The cDNA sequence of SEQ ID NO: 455 encodes the same polypeptide sequence as the cDNA sequence of SEQ ID NO: 359, namely SEQ ID NO: 383.

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Comparison of the polypeptide sequences corresponding to the cDNA sequences of SEQ ID NOS: 49-63, 250-253, 436 and 452 with those in the SwissProt database showed less than 75% identity (determined as described above) to known sequences. These polypeptide sequences are provided in SEQ ID NOS: 168-182, 327-330, 457 and 462, respectively.

Using automated search programs to screen against sequences coding for molecules reported to be of therapeutic and/or diagnostic use, some of the cDNA sequences isolated as described above in Example 1 were determined to encode polypeptides that are family members of known protein families. A family member is here defined to have at least 25% identity in the translated polypeptide to a known protein or member of a protein family. These cDNA sequences are provided in SEQ ID NOS: 64-76, 254-264, 365-369, 403, 437-439, 453, 454, 475-487, 510, 511, 514-527, 529-531, 533-536, 538-546, 548, 549, 553-559, 562, 564, 565, 567, 569-575, 577-589, 591-602, 604-612, 616-618, 621 and 622. The polypeptide sequences encoded by the cDNA sequences of SEQ ID NO: 64-76, 254-264, 365-369, 403, 438, 439, 453, 475-487, 510 and 511, 514-527, 529-531, 533-536, 538-546, 548, 549, 553-559, 562, 564, 565, 567, 569-575, 577-589, 591-602, 604-612, 616-618, 621 and 622 are provided in SEQ ID NOS: 183-195, 331-341, 389-393, 409, 458, 459, 463, 497-509, 624-637, 639-641, 643-

646, 648-656, 658, 659, 662-668, 670, 672-681, 683-707, 709-717 and 721-725, respectively. The cDNA sequences of SEQ ID NO: 437 and 454 encode the same amino acid sequences as the cDNA sequences of SEQ ID NO: 68 and 262, namely SEQ ID NO: 187 and 339, respectively. The cDNA sequences of SEQ ID NOS: 64-68, 254-264, 365-369, 437-439, 453, 454, 475-478, 480-482, 484, 485, 487, 511, 514, 515, 517-520, 522, 523, 525, 529-531, 535, 536, 538, 541, 544-546, 549, 553-559, 564, 565, 567, 569-573, 579, 587, 588, 592, 597, 598, 602, 604, 605, 608-611, 617, 621 and 622 show less than 75% identity (determined as described above) to sequences in the EMBL database using the FASTA or BLASTN computer algorithms. Similarly, the amino acid sequences of SEQ ID NOS: 183-195, 331-341, 389-393, 458, 459, 463, 497, 498, 503-505, 507-509, 512, 513, 628, 632, 633, 637, 640, 655, 662-666, 668, 672, 673, 676, 679, 683, 685, 688, 691, 693, 694, 702, 703, 706, 707, 710, 711, 713, 714, 717, 721, 722 and 725 show less than 75% identity to sequences in the SwissProt database.

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The isolated cDNA sequences encode proteins that influence the growth, differentiation and activation of several cell types, and that may usefully be developed as agents for the treatment and diagnosis of skin wounds, cancers, growth and developmental defects, and inflammatory disease. The utility for certain of the proteins of the present invention, based on similarity to known proteins, is provided in Table 2 below, together with the location of signal peptides and transmembrane domains for certain of the inventive sequences:

Table 2
FUNCTIONS OF NOVEL PROTEINS

P/N	A/A SEQ.	and the second s
SEQ ID	ID NO.	SIMILARITY TO KNOWN PROTEINS; FUNCTION
NO:		
64,	183,	Slit, a secreted molecule required for central nervous system
372	396	development
65	184	Immunoglobulin receptor family. About 40% of leucocyte
ļ		membrane polypeptides contain immunoglobulin
		superfamily domains

P/N	A/A SEQ.	
SEQ ID	ID NO.	SIMILARITY TO KNOWN PROTEINS; FUNCTION
NO:		<u> </u>
66,	185,	RIP protein kinase, a serine/threonine kinase that contains a
403	409	death domain to mediate apoptosis
510	512	
67	186	Extracellular protein with epidermal growth factor domain capable of stimulating fibroblast proliferation
68,	187	Transforming growth factor alpha, a protein which binds
437		epidermal growth factor receptor and stimulates growth and mobility of keratinocytes
69	188	DRS protein which has a secretion signal component and
		whose expression is suppressed in cells transformed by
		oncogenes
70	189	A33 receptor with immunoglobulin-like domains and is
		expressed in greater than 95% of colon tumors
71	190	Interleukin-12 alpha subunit, component of a cytokine that
-		is important in the immune defense against intracellular
		pathogens. IL-12 also stimulates proliferation and
		differentiation of TH1 subset of lymphocytes
72	191	Tumor Necrosis Factor receptor family of proteins that are
1	1	involved in the proliferation, differentiation and death of
	100	many cell types including B and T lymphocytes.
73	192	Epidermal growth factor family proteins which stimulate
		growth and mobility of keratinocytes and epithelial cells.
		EGF is involved in wound healing. It also inhibits gastric acid secretion.
74	193	Fibronectin Type III receptor family. The fibronectin III
/4	193	domains are found on the extracellular regions of cytokine
		receptors
75	194	Serine/threonine kinases (STK2_HUMAN) which
	1	participate in cell cycle progression and signal transduction
76	195	Immunoglobulin receptor family
254	331	Receptor with immunoglobulin-like domains and homology
1 20.	1	to A33 receptor which is expressed in greater than 95% of
		colon tumors
255	332	Epidermal growth factor family proteins which stimulate
}		growth and mobility of keratinocytes and epithelial cells.
		EGF is involved in wound healing. It also inhibits gastric
		acid secretion.
256	333	Serine/threonine kinases (STK2_HUMAN) which
		participate in cell cycle progression and signal transduction

P/N	A/A SEQ.	CD CT A DISTRICT OF A DISTRICT OF THE DESCRIPTION O
SEQ ID NO:	ID NO.	SIMILARITY TO KNOWN PROTEINS; FUNCTION
- 257	334	Contains protein kinase and ankyrin domains. Possible role in cellular growth and differentiation.
258	335	Notch family proteins which are receptors involved in cellular differentiation.
259	336	Extracellular protein with epidermal growth factor domain capable of stimulating fibroblast proliferation.
260, 453	337, 463	Fibronectin Type III receptor family. The fibronectin III domains are found on the extracellular regions of cytokine
261	338	receptors. Immunoglobulin receptor family
262	339	ADP/ATP transporter family member containing a calcium binding site.
263	340	Mouse CXC chemokine family members are regulators of epithelial, lymphoid, myeloid, stromal and neuronal cell migration and cancers, agents for the healing of cancers, neuro-degenerative diseases, wound healing, inflammatory autoimmune diseases like psoriasis, asthma, Crohns disease and as agents for the prevention of HIV-1 of leukocytes
264	341	Nucleotide-sugar transporter family member.
365	389	Transforming growth factor betas (TGF-betas) are secreted covalently linked to latent TGF-beta-binding proteins (LTBPs). LTBPs are deposited in the extracellular matrix and play a role in cell growth or differentiation.
366	390	Integrins are Type I membrane proteins that function as laminin and collagen receptors and play a role in cell adhesion.
367	391	Integrins are Type I membrane proteins that function as laminin and collagen receptors and play a role in cell adhesion.
368	392	Cell wall protein precursor. Are involved in cellular growth or differentiation.
369	393	HT protein is a secreted glycoprotein with an EGF-like domain. It functions as a modulator of cell growth, death or differentiation.
467	489	Myb proto-oncogene (c-Myb), involved in transcription regulation and activation of transcription

P/N	A/A SEQ.	
SEQ ID NO:	ID NO.	SIMILARITY TO KNOWN PROTEINS; FUNCTION
471	493	Chondroitin sulfotransferase, a member of the HNK-1 sulfotransferase family. These molecules are involved in the pathogenesis of arteriosclerosis, and proliferation of arterial smooth muscle cells during development of arteriosclerosis.
472	494	36 kDa nucleolar protein HNP36, a novel growth factor responsive gene expressed in the pituitary and parathyroid glands
475	497 .	Zinc protease is a matrix metalloproteinase whose activity is directed against components of the extracellular matrix and play an important role in the growth, metastasis and angiogenesis of tumors.
476	498	Diapophytoene dehydrogenase crtn-like molecule. This molecule is similar to the diapophytoene dehydrogenase crt molecule in a major photosynthesis gene cluster from the bacterium <i>Heliobacillus mobilis</i>
477	499	Protocadherin 3 family member, involved in cell to cell interactions.
478	500	Integrins are Type I membrane proteins that function as laminin and collagen receptors and play a role in cell adhesion.
479 .	501	Integrin family member. Integrins are Type I membrane proteins that function as laminin and collagen receptors and play a role in cell adhesion.
480	502	Similar to secreted HT Protein, a secreted glycoprotein with an EGF-like domain. It functions as a modulator of cell growth, death or differentiation.
481	503	Agrin family member: Agrin is produced by motoneurons and induces the aggregation of nicotinic acetylcholine receptors.
482	504	Macrophage Scavenger Receptors bind to a variety of polyanionic ligands and display complex binding characteristics. They have been implicated in various macrophage-associated processes, including atherosclerosis.
483	505	Similar to GARP, a member of the family of leucine-rich repeat-containing proteins involved in platelet-endothelium interactions.
484	506	Epidermal growth factor family proteins which stimulate growth and mobility of keratinocytes and epithelial cells. EGF is involved in wound healing. It also inhibits gastric

P/N SEQ ID	A/A SEQ. ID NO.	SIMILARITY TO KNOWN PROTEINS; FUNCTION
NO:	ID NO.	Shunearit termowith Releases, PolyCiton
		acid secretion.
485	507	Colony stimulating growth factor family.
486	508	Cytokine receptors
487	509	IL17 Receptor to Interleukin 17 (IL17), a T cell derived cytokine that may play a role in initiation or maintenance of the inflammatory response.
438	458	MEGF6, a protein containing multiple EGF-like-domains.
439	459	Protein kinase family member involved in signal transduction.
454		Peroxisomal calcium-dependent solute carrier, a new member of the mitochondrial transporter superfamily.
511	513	Serine/threonine kinase NEK1 is a NIMA-related protein kinase that phosphorylates serines and threonines, but also possesses tyrosine kinase activity. NEK1 has been implicated in the control of meiosis and belongs to the NIMA kinase subfamily.
514		6Homologue isolated from rat dermal papilla of integrin alpha-11/beta-1 that is involved in muscle development and maintaining integrity of adult muscle and other adult tissues. Integrin alpha-11/beta-1 is a receptor for collagen and belongs to the integrin alpha chain family.
516	625	This is a secreted molecule isolated from rat dermal papillae with a signal peptide at the N-terminus (amino acid residues 1 to 21; nucleotides 42 to 104).
517	626	Homologue isolated from a rat dermal papilla library of OASIS (old astrocyte specifically-induced substance) and that plays a role in regulation of the response of astrocytes to inflammation and trauma of the central nervous system (CNS) during gliosis. The OASIS gene encodes a putative transcription factor belonging to the cyclic AMP responsive element binding protein/activating transcription factor (CREB/ATF) gene family (Honma et al., Brain Res. Mol. Brain Res. 69:93-103, 1999).

P/N SEQ ID NO:	A/A SEQ. ID NO.	SIMILARITY TO KNOWN PROTEINS; FUNCTION
519	628	This is a secreted molecule isolated from rat dermal papillae with a signal peptide at the N-terminus (amino acid residues 1 to 24; nucleotides 50 to 121).
520	630	This is a secreted molecule isolated from rat dermal papillae with a signal peptide at the N-terminus (amino acid residues 1 to 35; nucleotides 67 to 171).
523	633	This is a secreted molecule isolated from rat dermal papillae with a signal peptide at the N-terminus (amino acid residues 1 to 17; nucleotides 3 to 53).
524	634	This is a secreted molecule isolated from rat dermal papillae with a signal peptide at the N-terminus (amino acid residues 1 to 20; nucleotides 13 to 72).
525, 534	635, 644	Homologue isolated from a rat dermal papilla library of leucyl-specific aminopeptidase, PILS-AP and that plays role in many physiological processes as a substrate-specific peptidase. PILS is a new member of the M1 famile of Zndependent aminopeptidases that comprises members of closely related enzymes which are known to be involved in a variety of physiologically important processes.
526	636	This is a secreted molecule isolated from rat dermal papillae with a signal peptide at the N-terminus (amino acid residues 1 to 26; nucleotides 114 to 191).
527	637	This is a secreted molecule isolated from rat dermal papillae with a signal peptide at the N-terminus (amino acid residues 1 to 26; nucleotides 23 to 100).
529	639	This is a secreted molecule isolated from rat dermal papillae with a signal peptide at the N-terminus (amino acid residues 1 to 17; nucleotides 37 to 87).
530	640	This is a homologue isolated from a rat dermal papilla library of a maturase that is involved in RNA splicing.
531	641	This is a secreted molecule isolated from rat dermal papillae with a signal peptide at the N-terminus (amino acid residues 1 to 17; nucleotides 180 to 230).
532	642	This is a secreted molecule isolated from rat dermal papillae with a signal peptide at the N-terminus (amino acid residues 1 to 32; nucleotides 245 to 340).
535	645	This is a secreted molecule isolated from rat dermal papillae with a signal peptide at the N-terminus (amino acid residues 1 to 25; nucleotides 188 to 333).

P/N	A/A SEQ.	CONTRACTOR AND ANALONIAL PROPERTY OF TAXABLE PROPERTY OF
SEQ ID NO:	ID NO.	SIMILARITY TO KNOWN PROTEINS; FUNCTION
536	646	This is a secreted molecule isolated from rat dermal papillae with a signal peptide at the N-terminus (amino acid residues 1 to 21; nucleotides 185 to 247).
537	647	This is a secreted molecule isolated from rat dermal papillae with a signal peptide at the N-terminus (amino acid residues 1 to 24; nucleotides 129 to 200).
541	651	This is a homologue isolated from a rat dermal papilla library of a hepatoma-derived growth factor (HDGF) that is involved in stimulation of cell proliferation.
542	652	This is a receptor-like molecule isolated from rat dermal papillae with two transmembrane domains (amino acid residues 20 to 40 and 58 to 78.
545	655	This is a homologue isolated from a rat dermal papilla library of Link protein (LP) and that is involved in bone formation. LP plays an essential role in endochondral bone formation by stabilizing the supramolecular assemblies of aggrecan and hyaluronan (Deak et al., Cytogenet. Cell Genet. 87:75-79, 1999).
548	658	This is a homologue isolated from a rat dermal papilla library of thrombospondin (TSP). It is a secreted protein with a signal peptide in amino acid residues 1 to 18 (nucleotides 210 to 263). TSP is an extracellular matrix glycoprotein whose expression has been associated with a variety of cellular processes including growth and embryogenesis (Laherty et al., J. Biol. Chem. 267:3,274-3,281, 1992).
553	662	This is a receptor-like molecule isolated from rat dermal papillae with a transmembrane domain (amino acid residues 434 to 454.
554	663	This is a receptor-like molecule isolated from rat dermal papillae with a transmembrane domain (amino acid residues 546 to 566.
555	664	This is a homologue isolated from a rat dermal papilla library of B7-like mouse GL50 (mGL50). It is a receptor-like molecule with a signal peptide in residues 1 to 24 (nucleotides 149 to 220) and a transmembrane domain in amino acid residues 262 to 282. GL50 is a specific ligand for the ICOS receptor and this interaction functions in lymphocyte costimulation (Ling et al., J. Immunol. 164:1,653-1,657, 2000).

P/N	A/A SEQ.	
SEQ ID NO:	ID NO.	SIMILARITY TO KNOWN PROTEINS; FUNCTION
557, 558, 561-572	666, 667, 670-678	These molecules are differentially expressed in stem cells but not in mature keratinocytes and are involved in developmental processes. They may be employed for diagnosis of tumors with an immature phenotype.
559	668	This is a homologue isolated from a mouse stem cell library of ABSENT IN MELANOMA 1 protein AIM1 and that can be used for diagnosis of tumours with an immature phenotype. AIM1 is a novel gene whose expression is associated with the experimental reversal of tumorigenicity of human malignant melanoma and belongs to the betagamma-crystallin superfamily (Ray et al., Proc. Natl. Acad. Sci. USA 94:3,229-3,234, 1997)
560	669	Homologue isolated from a mouse stem cell library of endothelin-convertin enzyme 2 (ECE-2) and that can be used for diagnosis of tumours with an immature phenotype. Endothelins (ET) are a family of potent vasoactive peptides that are produced from biologically inactive intermediates, termed big endothelins, via a proteolytic processing at Trp21-Val/Ile22. ECE-2, that produces mature ET-1 from big ET-1 both in vitro and in transfected cells. ECE-2 acts as an intracellular enzyme responsible for the conversion of endogenously synthesized big ET-1 at the trans-Golgi network, where the vesicular fluid is acidified (Emoto and Yanagisawa, J. Biol. Chem. 270:15,262-15,268, 1995).
573	679	Mouse homologue of EGF-like molecule containing mucin-like hormone receptor 2 (EMR2). The isolated molecule contains three transmembrane regions: amino acid residues 20 to 40, 66 to 86 and 92 to 112. The epidermal growth factor (EGF)-TM7 proteins [EMR1 and EMR2, F4/80, and CD97] constitute a recently defined class B GPCR subfamily and are predominantly expressed on leukocytes. These molecules possess N-terminal EGF-like domains coupled to a seven-span transmembrane (7TM) moiety via a mucin-like spacer domain (Lin et al., Genomics 67:188-200, 2000).
574	680	This is a murine secreted molecule with a signal peptide at the N-terminus (amino acid residues 1 to 17; nucleotides 238 to 288).
575	681	Mouse homologue of a glucocortocoid-inducible protein GIS5 with a signal peptide at the N-terminus (amino acid

P/N	A/A SEQ.		
SEQ ID NO:	ID NO.	SIMILARITY TO KNOWN PROTEINS; FUNCTION	
NO.		residues 1 to 17; nucleotides 56-106).	
)	
576	682	This is a murine surface receptor-like molecule with a signal peptide at the N-terminus (amino acid residues 1 to 17; nucleotides 1179 to 199) and a transmembrane domain (amino acid residues 179 to 199).	
577	683	This is a murine secreted molecule with a signal peptide at the N-terminus (amino acid residues 1 to 16; nucleotides 55 to 102).	
578	684	This is a murine secreted molecule with a signal peptide at the N-terminus (amino acid residues 1 to 22; nucleotides 12 to 77).	
579	685	This is a murine secreted molecule with a signal peptide at the N-terminus (amino acid residues 1 to 17; nucleotides 82 to 132).	
580	686	This is a murine secreted molecule with a signal peptide at the N-terminus (amino acid residues 1 to 20; nucleotides 20 to 79).	
581	687	This is a murine receptor-like molecule with transmembrane domains at amino acid residues 50 to 70; 84 to 104; 116 to 136 and 179 to 198.	
585	691	This is a murine secreted molecule with a signal peptide at the N-terminus (amino acid residues 1 to 20; nucleotides 260 to 319).	
586	695	This is a murine secreted molecule with a signal peptide at the N-terminus (amino acid residues 1 to 22; nucleotides 295 to 360).	
587		This is a mouse homologue of serotransferrin, also known as siderophilin or beta-1-metal binding globulin) and that is involved in iron transport. This homologue is a secreted molecule with a signal peptide at the N-terminus (amino acid residues 1 to 19; nucleotides 43 to 99). Transferrins are iron binding transport proteins which can bind two atoms of ferric iron in association with the binding of an anion, usually bicarbonate. It is responsible for the transport of iron from sites of absorption and heme degradation to those of storage and utilization. Serum transferrin may also have a further role in stimulating cell proliferation. Transferrin belongs to the transferrin family.	

P/N SEQ ID NO:	A/A SEQ. ID NO.	SIMILARITY TO KNOWN PROTEINS; FUNCTION
589	695	This is a murine secreted molecule with a signal peptide at the N-terminus (amino acid residues 1 to 25; nucleotides 1 to 75).
. 592	697	This is a murine receptor-like molecule with a transmembrane domain in amino acid residues 52 to 72.
593	698	Mouse homologue of channel inducing factor (CHIF) that plays a role in ion transport. The mouse homologue has a signal peptide at the N-terminus of the predicted polypeptide (amino acid residues 1 to 20; nucleotides 102 to 161) and a transmembrane domain (amino acid residues 38 to 58). CHIF evokes a potassium channel activity (Attali et al., Proc. Natl. Acad. Sci. USA 92:6092-6096, 1995).
595	700	Homologue of hyaluronan receptor LYVE-1 that plays a role in hyalyronan uptake. This mouse homologue has the characteristic signal peptide and transmembrane domain of a receptor. A signal peptide was identified in the isolated molecule in amino acid residues 1 to 18 (nucleotides 62 to 115) and the transmembrane domain in amino acid residues 233 to 253. The extracellular matrix glycosaminoglycan hyaluronan (HA) is an abundant component of skin and mesenchymal tissues where it facilitates cell migration during wound healing, inflammation, and embryonic morphogenesis. Both during normal tissue homeostasis and particularly after tissue injury, HA is mobilized from these sites through lymphatic vessels to the lymph nodes where it is degraded before entering the circulation for rapid uptake by the liver. LYVE-1 is a receptor for HA on the lymph vessel wall and plays a role in the transport of HA from tissue to lymph (Banerji et al., J. Cell Biol. 144:789-801,1999).
596	701	This is a murine secreted molecule with a signal peptide at the N-terminus (amino acid residues 1 to 21; nucleotides 7 to 69).
598	703	Homologue of tumor-associated glycoprotein E4 (TAA1 or TAGE4) that belongs to the immunoglobulin superfamily. This molecule has a signal peptide at the N-terminus (amino acid residues 1 to 24; nucleotides 71 to 142) and is therefore a secreted protein.

P/N	A/A SEQ.		
SEQ ID NO:	ID NO.	SIMILARITY TO KNOWN PROTEINS; FUNCTION	
599	704	Homologue of the LUNX protein, also known as nasopharyngeal carcinoma-related protein, tracheal epithelium enriched protein or plunc, that is expressed in epithelial cells in the airways. It has a signal peptide at the N-terminus (amino acid residues 1 to 19; nucleotides 39 to 95). Expression of LUNX is restricted to the trachea, upper airway, nasopharyngeal epithelium and salivary gland (Bingle and Bingle, Biochim. Biophys. Acta 1493:363-367, 2000).	
600	705	This is a murine secreted molecule with a signal peptide at the N-terminus (amino acid residues 1 to 23; nucleotides 136 to 204.	
601	706	Homologue of prenylcysteine lyase (EC 4.4.1.18) and that is involved in degradation of prenylated proteins. It has a signal peptide at the N-terminus (amino acid residues 1 to 28; nucleotides 22 to 105). Prenylcysteine lyase is a specific enzyme involved in the final step of prenylcysteine metabolism in mammalian cells. The enzyme does not require NADPH as cofactor for prenylcysteine degradation, thus distinguishing it from cytochrome P450- and flavincontaining monooxygenases that catalyze S-oxidation of thioethers (Zhang et al., J. Biol. Chem. 274:35802-35808, 1999).	
605	710	Homologue of endoplasmin, endoplasmic reticulum protein 99 (ERp99), 94 kDa glucose-regulated protein (GRP94) and polymorphic tumor rejection antigen 1 (gp96). The isolated molecule has a signal peptide at the N-terminus (amino acid residue 1 to 21; nucleotides 1867 to 206). ERp99 is an abundant, conserved transmembrane glycoprotein of the endoplasmic reticulum membrane and homologous to the 90-kDa heat shock protein (hsp90) and the 94-kDa glucose regulated protein (GRP94) (Mazzarella and Green, J. Biol. Chem. 262:8875-8883, 1987).	
606	711	Homologue of PILRalpha, formerly known as inhibitory receptor PIRIIalpha and that is involved in signal transduction in various cellular processes. This molecule contains a signal peptide at the N-terminal end (amino acid residues 1-21 and nucleotides 47 to 139) and a transmembrane domain at amino acid residues 191 to 211. SHP-1-mediated dephosphorylation of protein tyrosine	

P/N SEQ ID NO:	A/A SEQ. ID NO.	SIMILARITY TO KNOWN PROTEINS; FUNCTION
		residues is central to the regulation of several cell signaling pathways. PILRalpha, a novel immunoreceptor tyrosine-based inhibitory motif-bearing protein, recruits SHP-1 upon tyrosine phosphorylation and is paired with the truncated counterpart PILRbeta (Mousseau et al., J. Biol. Chem. 275:4467-4474, 2000).
607	712	This is a murine secreted molecule with a signal peptide at the N-terminus (amino acid residues 1 to 18; nucleotides 38 to 91.
609	714	Homologue of retinal short-chain dehydrogenase/reductase retSDR2 that plays a role on retinal metabolism. It has a signal peptide at the N-terminus at amino acid residues 1 – 29 (nucleotides 302 to 388). Retinol dehydrogenases (RDH) catalyze the reduction of all-trans-retinal to all-transretinol within the photoreceptor outer segment in the regeneration of bleached visual pigments (Haeseleer et al., J. Biol. Chem. 273:21790-21799, 1998)
612	717	This is a murine secreted molecule with a signal peptide at the N-terminus (amino acid residues 1 to 22; nucleotides 6 to 71.
613	718	This is a murine secreted molecule with a signal peptide at the N-terminus (amino acid residues 1 to 25; nucleotides 210 to 284.
615	720	This is a murine secreted molecule with a signal peptide at the N-terminus (amino acid residues 1 to 16; nucleotides 70 to 117.
616	721	This is a murine secreted molecule with a signal peptide at the N-terminus (amino acid residues 1 to 18; nucleotides 1 to 54.

The locations of open reading frames (ORFs) within certain of the inventive cDNA sequences are shown in Table 3, below.

Table 3

LOCATION OF OPEN READING FRAMES

5

SEQ ID NO Polynucleotide	ORF	SEQ ID NO Polypeptide
514	1-2,067	624
515	2-730	625
516	42-1,772	626
517	1-681	627
. 518	170-416	628
519	50-770	629
520	67-708	630
521	110-613	631
522	41-457	632
523	3-230	633
524	13-573	634
525	64-2,856	635
526	114-599	636
527	23-520	637
528	953-1,138	638
529	37-687	639
530	145-366	640
531	180-1,508	643
532	245-442	642
533	125-595	643
534	64-2,856	644
535	188-727	645
536	185-1,081	646
537	129-308	647
538	32-853	648
539	2-268	649
540	3-875	650
541	284-892	651
542	37-276	652
543	127-1,794	653
544	1-735	654
545	142-939	655
546	51-1,082	656
547	143-328	657
548	210-3,728	658
549	26-1,354	659
551	1,236-1,892	660
552	853-1,178	661

SEQ ID NO Polynucleotide	ORF	SEQ ID NO Polypeptide
553	54-1,356	662
554	637-2,244	663
555	149-1,072	664
556	18-449	665
557	275-1,171	666
558	453-1,133	667
559	104-2,449	668
560	463-687	669
562	1-1,107	670
563	2-883	671
564	188-2,902	672
565	3-524	673
567	2,584-3,996	674
569	1-960	675
570	315-599	676
571	1-414	677
572	806-1,912	678
573	120-752-	679
574	2381,359	680
575	56-1,456	681
576	13-645	682
577	55-1,323	683
578	12-698	684
579	82-810	685
580	20-586	686
581	65-808	687
582	369-761	688
583	1-769	689
584	164-1,321	690
585	260-1,489	691
586	295-1,131	692
587	43-2,136	. 693
588	1-1,203	694
589	1-525	695
591	1-584	696
592	1-522	697
593	102-368	698
594	1-517	699

SEQ ID NO		SEQ ID NO
Polynucleotide	ORF	Polypeptide
595	62-1,018	700
596	7-282	701
597	1-736	702
598	71-1,297	703
599	39-875	704
600	136-930	705
601	22-1,539	706
602	69-521	707
603	104-448	708
604	1-399	709
605	3,068-5,476	710
606	47-721	711
607	38-439	712
608	1-1,656	713
609	302-1,327	714
610	845-1,447	715
611	975-1,375	716
612	6-272	717
613	210-464	718
614	462-869	719
615	70-459	720
616	1-1,107	721
617	1-349	722
618	93-528	723
621	380-1,033	724
622	43-2,115	725

The cDNA sequences of SEQ ID NO: 514, 515, 516, 557, 558, 559, 560, 561, 567, 568, 619 and 621 are extended sequences of SEQ ID NO: 479, 480, 353, 91, 108, 82, 92, 81, 105, 90, 362 and 360, respectively. SEQ ID NO: 516, 520, 521, 523, 525, 526, 529, 534-536, 541-543, 546, 548, 549, 557, 574, 575, 577-581, 584-587, 589, 593, 595, 596, 598-601, 605, 607, 609, 610, 614, 616 and 622 represent full-length cDNA sequences.

The polynucleotide sequences of SEQ ID NOS: 77-117, 265-267, 404-405 and 557-611 are differentially expressed in either keratinocyte stem cells (KSCL) or in transit amplified cells (TRAM) on the basis of the number of times these sequences exclusively appear in either one of the above two libraries; more than 9 times in one and none in the other (Audic S. and Claverie J-M, *Genome Research*, 7:986-995, 1997). The sequences of SEQ ID NOS: 77-89, 265-267 and 365-369 were determined to have less than 75% identity to sequences in the EMBL database using the computer algorithm FASTA or BLASTN, as described above. The polypeptide sequences encoded by the cDNA sequences of SEQ ID NO: 77-117, 265-267, 404-405 and 557-611 are provided in SEQ ID NOS: 666-718. The amino acid sequences of SEQ ID NOS: 666, 668, 669, 671-673, 675, 676, 679, 682, 683, 685, 688, 690, 691, 693, 694, 702, 703, 706-708, 710, 711, 713 and 714 show less than 75% identity to sequences in the SwissProt database.

The polypeptides encoded by these polynucleotide sequences have utility as markers for identification and isolation of these cell types, and antibodies against these proteins may be usefully employed in the isolation and enrichment of these cells from complex mixtures of cells. Isolated polynucleotides and their corresponding proteins exclusive to the stem cell population can be used as drug targets to cause alterations in regulation of growth and differentiation of skin cells, or in gene targeting to transport specific therapeutic molecules to skin stem cells.

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Example 3

ISOLATION AND CHARACTERIZATION OF THE HUMAN HOMOLOG OF MUTR 1

The human homolog of muTR1 (SEQ ID NO: 68), obtained as described above in Example 1, was isolated by screening 50,000 pfu's of an oligo dT primed HeLa cell cDNA library. Plaque lifts, hybridization, and screening were performed using standard molecular biology techniques (Sambrook, J, Fritsch, EF and Maniatis, T, eds., *Molecular Cloning: A Laboratory Manual*, 2nd ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor: New York, 1989). The determined cDNA sequence of the isolated human homolog (huTR1) is provided in SEQ ID NO: 118, with the corresponding

polypeptide sequence being provided in SEQ ID NO: 196. The library was screened using an [α^{32} P]-dCTP labeled double stranded cDNA probe corresponding to nucleotides 1 to 459 of the coding region within SEQ ID NO: 118.

**The polypeptide sequence of huTR1 has regions similar to Transforming Growth Factor-alpha, indicating that this protein functions like an epidermal growth factor (EGF). EGF family members exist in a functional form as small peptides. Alignment of the functional peptides of the EGF family with SEQ ID NO: 196 revealed that an internal segment of SEQ ID NO: 196 (amino acids 54-104) shows greater than 40% identity to the active peptides of EGF, TGF-alpha and Epiregulin. The active peptides of the EGF family are sufficient for activity and contain several conserved residues critical for the maintenance of this activity. These residues are retained in huTR1. This EGF-like protein will serve to stimulate keratinocyte growth and motility, and to inhibit the growth of epithelial-derived cancer cells. This novel gene and its encoded protein may thus be used as agents for the healing of wounds and regulators of epithelial-derived cancers.

Analysis of RNA transcripts by Northern Blotting

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Northern analysis to determine the size and distribution of mRNA for huTR1 was performed by probing human tissue mRNA blots (Clontech) with a probe comprising nucleotides 93-673 of SEQ ID NO: 118, radioactively labeled with $[\alpha^{32}P]$ -dCTP. Prehybridization, hybridization, washing and probe labeling were performed as described in Sambrook, *et al.*, *Ibid.* mRNA for huTR1 was 3.5-4kb in size and was observed to be most abundant in heart and placenta, with expression at lower levels being observed in spleen, thymus, prostate and ovary (Fig. 1).

The high abundance of mRNA for huTR1 in the heart and placenta indicates a role for huTR1 in the formation or maintenance of blood vessels, as heart and placental tissues have an increased abundance of blood vessels, and therefore endothelial cells, compared to other tissues in the body. This, in turn, demonstrates a role for huTR1 in angiogenesis and vascularization of tumors. This is supported by the ability of

Transforming Growth Factor-alpha and EGF to induce *de novo* development of blood vessels (Schreiber, *et al.*, *Science* 232:1250-1253, 1986) and stimulate DNA synthesis in endothelial cells (Schreiber, *et al.*, *Science* 232:1250-1253, 1986), and their over-expression in a variety of human tumors.

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Purification of muTR1 and huTR1

Polynucleotides 177-329 of muTR1 (SEQ ID NO: 268), encoding amino acids 53-103 of muTR1 (SEQ ID NO: 342), and polynucleotides 208-360 of huTR1 (SEQ ID NO: 269), encoding amino acids 54-104 of huTR1 (SEQ ID NO: 343), were cloned into the bacterial expression vector pProEX HT (BRL Life Technologies), which contains a bacterial leader sequence and N-terminal 6xHistidine tag. These constructs were transformed into competent XL1-Blue *E. coli* as described in Sambrook et al., *Ibid*.

Starter cultures of these recombinant XL1-Blue E. coli were grown overnight at 37°C in Terrific broth containing 100 µg/ml ampicillin. This culture was spun down and used to inoculate 500 ml culture of Terrific broth containing 100 µg/ml ampicillin. Cultures were grown until the OD_{595} of the cells was between 0.4 and 0.8, whereupon IPTG was added to 1 mM. Cells were induced overnight and bacteria were harvested by centrifugation.

Both the polypeptide of muTR1 (SEQ ID NO: 342; referred to as muTR1a) and that of huTR1 (SEQ ID NO: 343; referred to as huTR1a) were expressed in insoluble inclusion bodies. In order to purify the polypeptides muTR1a and huTR1a, bacterial cell pellets were re-suspended in lysis buffer (20 mM Tris-HCl pH 8.0, 10 mM beta mercaptoethanol, 1 mM PMSF). To the lysed cells, 1% NP40 was added and the mix incubated on ice for 10 minutes. Lysates were further disrupted by sonication on ice at 95W for 4 x 15 seconds and then centrifuged for 15 minutes at 14,000 rpm to pellet the inclusion bodies.

The resulting pellet was re-suspended in lysis buffer containing 0.5% w/v CHAPS and sonicated on ice for 5-10 seconds. This mix was stored on ice for 1 hour, centrifuged at 14,000 rpm for 15 minutes at 4 °C and the supernatant discarded. The pellet was once

more re-suspended in lysis buffer containing 0.5% w/v CHAPS, sonicated, centrifuged and the supernatant removed as before. The pellet was re-suspended in solubilizing buffer (6 M Guanidine HCl, 0.5 M NaCl, 20 mM Tris HCl, pH 8.0), sonicated at 95 W for 4 x 15 seconds and then centrifuged for 20 minutes at 14,000 rpm and 4 °C to remove debris. The supernatant was stored at 4 °C until use.

Polypeptides muTR1a and huTR1a were purified by virtue of the N-terminal 6x Histidine tag contained within the bacterial leader sequence, using a Nickel-Chelating Sepharose column (Amersham Pharmacia, Uppsala, Sweden) and following the manufacturer's recommended protocol. In order to refold the proteins once purified, the protein solution was added to 5x its volume of refolding buffer (1 mM EDTA, 1.25 mM reduced glutathione, 0.25 mM oxidised glutathione, 20 mM Tris-HCl, pH 8.0) over a period of 1 hour at 4 °C. The refolding buffer was stirred rapidly during this time, and stirring continued at 4 °C overnight. The refolded proteins were then concentrated by ultrafiltration using standard protocols.

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Biological Activities of Polypeptides muTR1a and huTR1a

muTR1 and huTR1 are novel members of the EGF family, which includes EGF, TGFα, epiregulin and others. These growth factors are known to act as ligands for the EGF receptor. The pathway of EGF receptor activation is well documented. Upon binding of a ligand to the EGF receptor, a cascade of events follows, including the phosphorylation of proteins known as MAP kinases. The phosphorylation of MAP kinase can thus be used as a marker of EGF receptor activation. Monoclonal antibodies exist which recognize the phosphorylated forms of 2 MAP kinase proteins – ERK1 and ERK2.

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In order to examine whether purified polypeptides of muTR1a and huTR1a act as a ligand for the EGF receptor, cells from the human epidermal carcinoma cell line A431 (American Type Culture Collection, No. CRL-1555, Manassas, Virginia) were seeded into 6 well plates, serum starved for 24 hours, and then stimulated with purified muTR1a or huTR1a for 5 minutes in serum free conditions. As a positive control, cells were

stimulated in the same way with 10 to 100 ng/ml TGF-alpha or EGF. As a negative control, cells were stimulated with PBS containing varying amounts of LPS. Cells were immediately lysed and protein concentration of the lysates estimated by Bradford assay. 15 µg of protein from each sample was loaded onto 12% SDS-PAGE gels. The proteins were then transferred to PVDF membrane using standard techniques.

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For Western blotting, membranes were incubated in blocking buffer (10mM Tris-HCl, pH 7.6, 100 mM NaCl, 0.1% Tween-20, 5% non-fat milk) for 1 hour at room temperature. Rabbit anti-Active MAP kinase pAb (Promega, Madison, Wisconsin) was added to 50 ng/ml in blocking buffer and incubated overnight at 4 °C. Membranes were washed for 30 mins in blocking buffer minus non-fat milk before being incubated with anti rabbit IgG-HRP antibody, at a 1:3500 dilution in blocking buffer, for 1 hour at room temperature. Membranes were washed for 30 minutes in blocking buffer minus non-fat milk, then once for 5 minutes in blocking buffer minus non-fat milk and 0.1% Tween-20. Membranes were then exposed to ECL reagents for 2 min, and then autoradiographed for 5 to 30 min.

As shown in Fig. 2, both muTR1a and huTR1a were found to induce the phosphorylation of ERK1 and ERK2 over background levels, indicating that muTR1 and huTR1 act as ligands for a cell surface receptor that activates the MAP kinase signaling pathway, possibly the EGF receptor. As shown in Fig. 11, huTR1a was also demonstrated to induce the phosphorylation of ERK1 and ERK2 in CV1/EBNA kidney epithelial cells in culture, as compared with the negative control. These assays were conducted as described above. This indicates that huTR1a acts as a ligand for a cell surface receptor that activates the MAP kinase signaling pathway, possibly the EGF receptor in HeLa and CV1/EBNA cells.

The ability of muTR1a to stimulate the growth of neonatal foreskin (NF) keratinocytes was determined as follows. NF keratinocytes derived from surgical discards were cultured in KSFM (BRL Life Technologies) supplemented with bovine pituatary extract (BPE) and epidermal growth factor (EGF). The assay was performed in 96 well flat-bottomed plates in 0.1 ml unsupplemented KSFM. MuTR1a, human

transforming growth factor alpha (huTGF α) or PBS-BSA was titrated into the plates and 1 x 10³ NF keratinocytes were added to each well. The plates were incubated for 5 days in an atmosphere of 5% CO₂ at 37⁰C. The degree of cell growth was determined by MTT dye reduction as described previously (*J. Imm. Meth.* 93:157-165, 1986). As shown in Fig. 3, both muTR1a and the positive control human TGF α stimulated the growth of NF keratinocytes, whereas the negative control, PBS-BSA, did not.

The ability of muTR1a and huTR1a to stimulate the growth of a transformed human keratinocyte cell line, HaCaT, was determined as follows. The assay was performed in 96 well flat-bottomed plates in 0.1 ml DMEM (BRL Life Technologies) supplemented with 0.2% FCS. MuTR1a, huTR1a and PBS-BSA were titrated into the plates and 1 x10³ HaCaT cells were added to each well. The plates were incubated for 5 days in an atmosphere containing 10% CO₂ at 37⁰C. The degree of cell growth was determined by MTT dye reduction as described previously (*J. Imm. Meth.* 93:157-165, 1986). As shown in Fig. 4, both muTR1a and huTR1a stimulated the growth of HaCaT cells, whereas the negative control PBS-BSA did not.

The ability of muTR1a and huTR1a to inhibit the growth of A431 cells was determined as follows. Polypeptides muTR1a (SEQ ID NO: 342) and huTR1a (SEQ ID NO: 343) and PBS-BSA were titrated as described previously (*J. Cell. Biol.* 93:1-4, 1982), and cell death was determined using the MTT dye reduction as described previously (*J. Imm. Meth.* 93:157-165, 1986). Both muTR1a and huTR1a were found to inhibit the growth of A431 cells, whereas the negative control PBS-BSA did not (Fig. 5).

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These results indicate that muTR1 and huTR1 stimulate keratinocyte growth and motility, inhibit the growth of epithelial-derived cancer cells, and play a rolê in angiogenesis and vascularization of tumors. This novel gene and its encoded protein may thus be developed as agents for the healing of wounds, angiogenesis and regulators of epithelial-derived cancers.

Upregulation of huTR1 and mRNA expression

HeLa cells (human cervical adenocarcinoma) were seeded in 10 cm dishes at a concentration of 1 x 10⁶ cells per dish. After incubation overnight, media was removed and replaced with media containing 100 ng/ml of muTR1, huTR1, huTGFα, or PBS as a negative control. After 18 hours, media was removed and the cells lysed in 2 ml of TRIzol reagent (Gibco BRL Life Technologies, Gaithersburg, Maryland). Total RNA was isolated according to the manufacturer's instructions. To identify mRNA levels of huTR1 from the cDNA samples, 1 μl of cDNA was used in a standard PCR reaction. After cycling for 30 cycles, 5 μl of each PCR reaction was removed and separated on a 1.5% agarose gel. Bands were visualized by ethidium bromide staining. As can be seen from Fig. 12, both mouse and human TR1 up-regulate the mRNA levels of huTR1 as compared with cells stimulated with the negative control of PBS. Furthermore, TGFα can also up-regulate the mRNA levels of huTR1.

These results indicate that TR1 is able to sustain its own mRNA expression and subsequent protein expression, and thus is expected to be able to contribute to the progression of diseases such as psoriasis where high levels of cytokine expression are involved in the pathology of the disease. Furthermore, since $TGF\alpha$ can up-regulate the expression of huTR1, the up-regulation of TR1 mRNA may be critical to the mode of action of $TGF\alpha$.

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Serum response element reporter gene assay

The serum response element (SRE) is a promoter element required for the regulation of many cellular immediate-early genes by growth. Studies have demonstrated that the activity of the SRE can be regulated by the MAP kinase signaling pathway. Two cell lines, PC12 (rat pheochromocytoma – neural tumor) and HaCaT (human transformed keratinocytes), containing eight SRE upstream of an SV40 promotor and luciferase reporter gene were developed in-house. 5 x 10³ cells were aliquoted per well of 96 well plate and grown for 24 hours in their respective media. HaCaT SRE cells were grown in 5% fetal bovine serum (FBS) in D-MEM supplemented with 2mM L-glutamine (Sigma,

St. Louis, Missouri), 1mM sodium pyruvate (BRL Life Technologies), 0.77mM L-asparagine (Sigma), 0.2mM arginine (Sigma), 160mM penicillin G (Sigma), 70mM dihydrostreptomycin (Roche Molecular Biochemicals, Basel, Switzerland), and 0.5 mg/ml geneticin (BRL Life Technologies). PC12 SRE cells were grown in 5% fetal bovine serum in Ham F12 media supplemented with 0.4 mg/ml geneticin (BRL Life Technologies). Media was then changed to 0.1% FBS and incubated for a further 24 hours. Cells were then stimulated with a titration of TR1 from 1 µg/ml. A single dose of basic fibroblast growth factor at 100 ng/ml (R&D Systems, Minneapolis, Minnesota) or epidermal growth factor at 10 ng/ml (BRL Life Technologies) was used as a positive control. Cells were incubated in the presence of muTR1 or positive control for 6 hours, washed twice in PBS and lysed with 40 µl of lysis buffer (Promega). 10 µl was transferred to a 96 well plate and 10 µl of luciferase substrate (Promega) added by direct injection into each well by a Victor² fluorimeter (Wallac), the plate was shaken and the luminescence for each well read at 3x1 sec Intervals. Fold induction of SRE was calculated using the following equation: Fold induction of SRE = Mean relative luminescence of agonist/Mean relative luminescence of negative control.

As shown in Fig. 13, muTR1 activated the SRE in both PC-12 (Fig. 13A) and HaCaT (Fig. 13B) cells. This indicates that HaCaT and PC-12 cells are able to respond to muTR1 protein and elicit a response. In the case of HaCaT cells, this is a growth response. In the case of PC-12 cells, this may be a growth, a growth inhibition, differentiation, or migration response. Thus, TR1 may be important in the development of neural cells or their differentiation into specific neural subsets. TR1 may also be important in the development and progression of neural tumors.

Inhibition by the EGF receptor assay

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The HaCaT growth assay was conducted as previously described, with the following modifications. Concurrently with the addition of EGF and TR1 to the media, anti-EGF Receptor (EGFR) antibody (Promega, Madison, Wisconsin) or the negative

control antibody, mouse IgG (PharMingen, San Diego, California), were added at a concentration of 62.5 ng/ml.

As seen in Fig. 14, an antibody which blocks the function of the EGFR inhibited the mitogenicity of TR1 on HaCaT cells. This indicates that the EGFR is crucial for transmission of the TR1 mitogenic signal on HaCaT cells. TR1 may bind directly to the EGF receptor. TR1 may also bind to any other members of the EGFR family (for example, ErbB-2, -3, and/or -4) that are capable of heterodimerizing with the EGFR.

Splice variants of huTR1

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A variant of huTR1 was isolated from the same library as huTR1, following the same protocols. The sequence referred to as huTR1-1 (also known as TR1δ) is a splice variant of huTR1 and consists of the ORF of huTR1 minus amino acids 15 to 44 and 87 to 137. These deletions have the effect of deleting part of the signal sequence and following amino terminal linker sequence, residues following the second cysteine residue of the EGF motif and the following transmembrane domain. However, cysteine residue 147 (huTR1 ORF numbering) may replace the deleted cysteine and thus the disulphide bridges are likely not affected. Therefore, huTR1-1 is an intracellular form of huTR1. It functions as an agonist or an antagonist to huTR1 or other EGF family members, including EGF and TGFα. The determined nucleotide sequence of huTR1-1, is given in SEQ ID NO: 412, with the corresponding amino acid sequence being provided in SEQ ID NO: 415.

Four additional splice variants of huTr1 were isolated by PCR on first strand cDNA made from RNA isolated from HeLa cells by standard protocols. These splice variants of huTR1 are referred to as TR1-2 (also known as TR1 β), TR1-3 (also known as TR1 γ), TR1 ϵ and TR1 ϕ .

TR1-2 consists of the ORF of huTR1 minus amino acids 95 to 137. This deletion has the effect of deleting the transmembrane domain. Therefore TR1-2 is a secreted form of huTR1 and binds with equal or greater affinity to the TR1 receptor as huTR1, since the EGF domain remains intact. It functions as an agonist or an antagonist to huTR1 or other

EGF family members, including EGF and TGFα. The determined cDNA sequence of TR1-2 is given in SEQ ID NO: 410 and the corresponding amino acid sequence in SEQ ID NO: 413.

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TR1-3 consists of the ORF of huTR1 minus amino acids 36 to 44 and amino acids 86 to 136. These deletions have the effect of deleting part of the amino terminal linker sequence, residues following the second cysteine of the EGF motif and the following transmembrane domain. However, cysteine residue 147 (huTR1 ORF numbering) may replace the deleted cysteine and thus the disulphide bridges are likely not affected. Therefore, TR1-3 is also a secreted form of huTR1 and functions as an agonist or an antagonist to huTR1 or other EGF family members, including EGF and TGFα. The determined cDNA sequence of TR1-3 is given in SEQ ID NO: 411 and the corresponding amino acid sequence is SEQ ID NO: 414.

TR1ε consists of the ORF of huTR1 minus amino acids 86 to 136. This deletion has the effect of deleting residues following the second cysteine of the EGF motif and the transmembrane domain. However, cysteine residue 147 (huTR1 ORF numbering) may replace the deleted cysteine and thus the disulphide bridges are likely not affected. Therefore, TR1ε is also a secreted form of huTR1 and functions as an agonist or an antagonist to huTR1 or other EGF family members, including EGF and TGFα. The determined cDNA sequence of TR1ε is given in SEQ ID NO: 371 and the corresponding polypeptide sequence in SEQ ID NO: 395.

TR1 ϕ consists of the ORF of huTR1 minus amino acids 36 to 44 and amino acids 95 to 136. These deletions have the effect of deleting part of the amino terminal linker sequence and the transmembrane domain. Therefore TR1 ϕ is a secreted form of huTR1 and binds with equal or greater affinity to the TR1 receptor as huTR1, since the EGF domain remains intact. It functions as an agonist or an antagonist to huTR1 or other EGF family members, including EGF and TGF α . The determined nucleotide sequence of TR1 ϕ is given in SEQ ID NO: 416 and the corresponding polypeptide sequence in SEQ ID NO: 417.

Example 4

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IDENTIFICATION, ISOLATION AND CHARACTERIZATION OF DP3

A partial cDNA fragment, referred to as DP3, was identified by differential display RT-PCR (modified from Liang P and Pardee AB, *Science* 257:967-971, 1992) using mRNA from cultured rat dermal papilla and footpad fibroblast cells, isolated by standard cell biology techniques. This double stranded cDNA was labeled with $[\alpha^{32}P]$ -dCTP and used to identify a full length DP3 clone by screening 400,000 pfu's of an oligo dT-primed rat dermal papilla cDNA library. The determined full-length cDNA sequence for DP3 is provided in SEQ ID NO: 119, with the corresponding amino acid sequence being provided in SEQ ID NO: 197. Plaque lifts, hybridization and screening were performed using standard molecular biology techniques.

Example 5 ISOLATION AND CHARACTERIZATION OF KS1

25 Analysis of RNA transcripts by Northern Blotting

Northern analysis to determine the size and distribution of mRNA for muKS1 (SEQ ID NO: 263) was performed by probing murine tissue mRNA blots with a probe consisting of nucleotides 268-499 of muKS1, radioactively labeled with $[\alpha^{32}P]$ -dCTP. Prehybridization, hybridization, washing, and probe labeling were performed as

described in Sambrook, et al., Ibid. mRNA for muKS1 was 1.6 kb in size and was observed to be most abundant in brain, lung, or any muscle, and heart. Expression could also be detected in lower intestine, skin, bone marrow, and kidney. No detectable signal was found in testis, spleen, liver, thymus, stomach.

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Human homologue of muKS1

MuKS1 (SEQ ID NO: 263) was used to search the EMBL database (Release 50, plus updates to June, 1998) to identify human EST homologues. The top three homologies were to the following ESTs: accession numbers AA643952, HS1301003 and AA865643. These showed 92.63% identity over 285 nucleotides, 93.64% over 283 nucleotides and 94.035% over 285 nucleotides, respectively. Frame shifts were identified in AA643952 and HS1301003 when translated. Combination of all three ESTs identified huKS1 (SEQ ID NO: 270) and translated polypeptide SEQ ID NO: 344. Alignment of muKS1 and huKS1 polypeptides indicated 95% identity over 96 amino acids.

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Identification of KSCL009274 cDNA sequence

A directionally cloned cDNA library was constructed from immature murine keratinocytes and submitted for high-throughput sequencing. Sequence data from a clone designated KDCL009274 showed 35% identity over 72 amino acids with rat macrophage inflammatory protein-2B (MIP-2B) and 32% identity over 72 amino acids with its murine homologue. The insert of 1633bp (SEQ ID NO: 464; Fig. 15A) contained an open reading frame of 300bp with a 5' untranslated region of 202bp and a 3' untranslated region of 1161bp. A poly-adenylation signal of AATAAA is present 19 base pairs upstream of the poly-A tail. The mature polypeptide (SEQ ID NO: 465) is 77 amino acids in length containing 4 conserved cysteines with no ELR motif. The putative signal peptide cleavage site beween GLY 22 and Ser 23 was predicted by the hydrophobicity profile. This putative chemokine was identical to KS1. The full length sequence was screened against the EMBL database using the BLAST program and showed some identity at the nucleotide level with human EST clones AA643952, AA865643, and

HS1301003, respectively. A recently described human CXC chemokine, BRAK, has some identity with KS1 at the protein level. The alignment of KS1 (referred to in Fig. 15B as KLF-1), BRAK, and other murine α -chemokines is shown in Fig. 15B. The phylogenetic relationship between KS1 and other α -chemokine family members was determiend using the Phylip program. KS1 and BRAK demonstrate a high degree of divergence from the other α -chemokines, supporting the relatively low homology shown in the multiple alignment.

Bacterial expression and purification of muKS1 and huKS1

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Polynucleotides 269-502 of muKS1 (SEQ ID NO: 271), encoding amino acids 23-99 of polypeptide muKS1 (SEQ ID NO: 345), and polynucleotides 55-288 of huKS1 (SEQ ID NO: 272), encoding amino acids 19-95 of polypeptide huKS1 (SEQ ID NO: 346), were cloned into the bacterial expression vector pET-16b (Novagen, Madison, Wisconsin), which contains a bacterial leader sequence and N-terminal 6xHistidine tag. These constructs were transformed into competent XL1-Blue *E. coli* as described in Sambrook et al., *Ibid*.

Starter cultures of recombinant BL 21 (DE3) *E. coli* (Novagen) containing SEQ ID NO: 271 (muKS1a) and SEQ ID NO: 272 (huKS1a) were grown in NZY broth containing 100 µg/ml ampicillin (Gibco-BRL Life Technologies) at 37°C. Cultures were spun down and used to inoculate 800 ml of NZY broth and 100 µg/ml ampicillin. Cultures were grown until the OD₅₉₅ of the cells was between 0.4 and 0.8. Bacterial expression was induced for 3 hours with 1 mM IPTG. Bacterial expression produced an induced band of approximately 15kDa for muKS1a and huKS1a.

MuKS1a and huKS1a were expressed in insoluble inclusion bodies. In order to purify the polypeptides, bacterial cell pellets were re-suspended in lysis buffer (20 mM Tris-HCl pH 8.0, 10 mM β Mercaptoethanol, 1 mM PMSF). To the lysed cells, 1% NP-40 was added and the mix incubated on ice for 10 minutes. Lysates were further disrupted by sonication on ice at 95 W for 4 x 15 seconds and then centrifuged for 10 minutes at 18,000 rpm to pellet the inclusion bodies.

The pellet containing the inclusion bodies was re-suspended in lysis buffer containing 0.5% w/v CHAPS and sonicated for 5-10 seconds. This mix was stored on ice for 1 hour, centrifuged at 14000 rpm for 15 minutes at 4°C and the supernatant discarded. The pellet was once more re-suspended in lysis buffer containing 0.5% w/v CHAPS, sonicated, centrifuged, and the supernatant removed as before. The pellet was resuspended in solubilizing buffer (6 M guanidine HCl, 0.5 M NaCl, 20 mM Tris-HCl pH 8.0), sonicated at 95W for 4 x 15 seconds and centrifuged for 10 minutes at 18000 rpm and 4°C to remove debris. The supernatant was stored at 4°C. MuKS1a and huKS1a were purified by virtue of the N-terminal 6x histidine tag contained within the bacterial leader sequence, using a Nickel-Chelating sepharose column (Amersham Pharmacia, Uppsala, Sweden) and following the manufacturer's protocol. Proteins were purified twice over the column to reduce endotoxin contamination. In order to re-fold the proteins once purified, the protein solution was dialysed in a 4 M-2 M urea gradient in 20 mM tris-HCl pH 7.5 + 10% glycerol overnight at 4°C. The protein was then further dialysed 2x against 2 litres of 20 mM Tris-HCl pH 7.5 + 10% (w/v) glycerol. Preparations obtained were greater than 95% pure as determined by SDS-PAGE. Endotoxin contamination of purified proteins were determined using a limulus amebocyte lysate assay kit (BIO Whittaker, Walkersville, MD). Endotoxin levels were <0.1 ng/µg of protein. Internal amino acid sequencing was performed on tryptic peptides of KS1.

An Fc fusion protein was produced by expression in HEK 293 T cells. 35µg of KLF-1plGFc DNA to transfect 6 x 10⁶ cells per flask, 200 mls of Fc containing supernatant was produced. The Fc fusion protein was isolated by chromatography using an Affiprep protein A resin (0.3 ml column, Biorad). After loading, the column was washed with 15 mls of PBS, followed by a 5 ml wash of 50 mM Na citrate pH 5.0. The protein was then eluted with 6 column volumes of 50 mM Na citrate pH 2.5, collecting 0.3 ml fractions in tubes containing 60µl of 2M Tris-HCI pH 8.0. Fractions were analyzed by SDS-PAGE.

Peptide sequencing of muKS1 and huKS1

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Bacterially expressed muKS1 and huKS1 were separated on polyacrylamide gels and induced bands of 15 kDa were identified. The predicted size of muKS1 is 9.4 kDa. To obtain the amino acid sequence of the 15 kDa bands, 20 µg recombinant muKS1 and huSK1 was resolved by SDS-PAGE and electroblotted onto Immobilon PVDF membrane (Millipore, Bedford, Massachusetts). Internal amino acid sequencing was performed on tryptic peptides of muKS1 and huKS1 by the Protein Sequencing Unit at the University of Auckland, New Zealand.

The determined amino acid sequences for muKS1 and huKS1 are given in SEQ ID NOS: 397 and 398, respectively. These amino acid sequences confirmed that the determined sequences are identical to those established on the basis of the cDNA sequences. The size discrepancy has previously been reported for other chemokines (Richmond A, Balentien E, Thomas HG, Flaggs G, Barton DE, Spiess J, Bordoni R, Francke U, Derynck R, "Molecular characterization and chromosomal mapping of melanoma growth stimulatory activity, a growth factor structurally related to beta-thromboglobulin," *EMBO J.* 7:2025-2033, 1988; Liao F, Rabin RL, Yannelli JR, Koniaris LG, Vanguri P, Farber JM, "Human Nig chemokine: biochemical and functional characterization," *J. Exp. Med.* 182:1301-1314, 1995). The isoelectric focusing point of these proteins was predicted to be 10.26 using DNASIS (HITACHI Software Engineering, San Francisco, California). Recombinant Fc tagged KS1 expresssed and purified using protein A affinity column chromatography revealed a homogenous protein with a molecular mass of 42kDa.

Oxidative burst assay

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Oxidative burst assays were used to determine responding cell types. 1×10^7 PBMC cells were resuspended in 5 ml HBSS, 20mM HEPES, 0.5% BSA and incubated for 30 minutes at 37°C with 5 μ l 5 mM dichloro-dihydrofluorescein diacetate (H₂DCFDA, Molecular Probes, Eugene, Oregon). 2×10^5 H₂DCFDA-labeled cells were loaded in each well of a flat-bottomed 96 well plate. 10 μ l of each agonist was added simultaneously into the well of the flat-bottomed plate to give final concentrations of 100 ng/ml (fMLP was used at 10 μ M). The plate was then read on a Victor² 1420

multilabel counter (Wallac, Turku, Finland) with a 485 nm excitation wavelength and 535 nm emission wavelength. Relative fluorescence was measured at 5 minute intervals over 60 minutes.

A pronounced respiratory burst was identified in PBMC with a 2.5 fold difference between control treated cells (TR1) and cells treated with 100 ng/ml muKS1 (Fig. 8). Human stromal derived factor- 1α (SDF1 α) (100 ng/ml) and 10 μ M formyl-Met-Leu-Phe (fMLP) were used as positive controls.

Chemotaxis assay

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Cell migration in response to muKS1 was tested using a 48 well Boyden's chamber (Neuro Probe Inc., Cabin John, Maryland) as described in the manufacturer's protocol. In brief, agonists were diluted in HBSS, 20mM HEPES, 0.5% BSA and added to the bottom wells of the chemotactic chamber. THP-1 cells were re-suspended in the same buffer at 3 x 10⁵ cells per 50 µ1. Top and bottom wells were separated by a PVP-free polycarbonate filter with a 5 µm pore size for monocytes or 3 µm pore size for lymphocytes. Cells were added to the top well and the chamber incubated for 2 hours for monocytes and 4 hours for lymphocytes in a 5% CO₂ humidified incubator at 37°C. After incubation, the filter was fixed and cells scraped from the upper surface. The filter was then stained with Diff-Quick (Dade International Inc., Miami, Florida) and the number of migrating cells counted in five randomly selected high power fields. The results are expressed as a migration index (the number of test migrated cells divided by the number of control migrated cells).

Using this assay, muKS1 was tested against T cells and THP-1 cells. MuKS1 induced a titrateable chemotactic effect on THP-1 cells from 0.01 ng/ml to 100 ng/ml (Fig. 9). Human SDF1 α was used as a positive control and gave an equivalent migration. MuKS1 was also tested against IL-2 activated T cells. However, no migration was evidence for muKS1 even at high concentrations, whereas SDF-1 α provided an obvious titrateable chemotactic stimulus. Therefore, muKS1 appears to be chemotactic for THP-1 cells but not for IL-2 activated T cells at the concentrations tested.

Flow cytometric binding studies

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Binding of KLF-1 to THP-1 and Jurkat cells was tested in the following manner. THP-1 or Jurkat cells (5 x 106) were resuspended in 3 mls of wash buffer (2% FBS and 0.2% sodium azide in PBS) and pelleted at 4°C, 200 x g for 5 minutes. Cells were then blocked with 0.5% mouse and goat sera for 30 minutes on ice. Cells were washed, pelleted, resuspended in 50 µl of KLF-1Fc at 10 µg/ml and incubated for 30 minutes on ice. After incubation, the cells were prepared as before and resuspended in 50 µl of goat anti-human IgG biotin (Southern Biotechnology Associates, AL) at 10 µg/ml and incuated for 30 minutes on ice. Finally, cells were washed, pelleted and resuspended in 50 ul of streptavidin-RPE (Southern Biotechnology Associates, AL) at 10 µg/ml and incuabated for a further 30 minutes on ice in the dark. Cells were washed and resuspended in 250 µl of wash buffer and stained with 1µl of 10 µg/ml propidium iodide (Sigma) to exclude any dead cells. Purified Fc fragment (10 µg/ml) was used as a negative control in place of KLF-1Fc to determine non-specific binding. Ten thousand gated events were analyzed on log scale using PE filter arrangement with peak transmittance at 575 nm and bandwidth of 10 nm on an Elite cell sorter (Coulter Cytometry).

The respiratory burst and migration assays indicated that KS1 is active on monocytes and not T cells; therefore, the KS1 Fc fusion protein was tested in a binding study with THP-1 and Jurkat T cells. KS1 Fc showed a marked positive shift on THP-1 cells compared with the Fc fragment alone. In contrast, KS1 demonstrated no positive binding with Jurkat cells in an identical experiment.

25 Full length sequence of muKS1 clone

The nucleotide sequence of muKS1 was extended by determining the base sequence of additional ESTs. Combination of all the ESTs identified the full-length muKS1 (SEQ ID NO: 370) and the corresponding translated polypeptide sequence in SEQ ID NO: 394.

Analysis of human RNA transcripts by Northern blotting

Northern blot analysis to determine the size and distribution of mRNA for the human homologue of muKS1 was performed by probing human tissue blots (Clontech, Palo Alto, California) with a radioactively labeled probe consisting of nucleotides 1 to 288 of huKS1 (SEQ ID NO: 270). Prehybridization, hybridization, washing, and probe labeling were performed as described in Sambrook, *et al.*, *Ibid.* mRNA for huKS1 was 1.6 kb in size and was observed to be most abundance in kidney, liver, colon, small intestine, and spleen. Expression could also be detected in pancreas, skeletal muscle, placenta, brain, heart, prostate, and thymus. No detectable signal was found in lung, ovary, and testis.

Analysis of human RNA transcripts in tumor tissue by Northern blotting

Northern blot analysis to determine distribution of huKS1 in cancer tissue was performed as described previously by probing tumor panel blots (Invitrogen, Carlsbad, California). These blots make a direct comparison between normal and tumor tissue. MRNA was observed in normal uterine and cervical tissue but not in the respective tumor tissue. In contrast, expression was up-regulated in breast tumor and down-regulated in normal breast tissue. No detectable signal was found in either ovary or ovarian tumors.

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Injection of bacterially recombinant muKS1 into C3H/HeJ mice

Eighteen C3H/HeJ mice were divided into 3 groups and injected intraperitoneally with muKS1, GV14B, or phosphate buffered saline (PBS). GV14B is a bacterially expressed recombinant protein used as a negative control. Group 1 mice were injected with 50 μg of muKS1 in 1 ml of PBS; Group 2 mice were injected with 50 μg of GV14B in 1 ml of PBS; and Group 3 mice with 1 ml of PBS. After 18 hours, the cells in the peritoneal cavity of the mice were isolated by intraperitoneal lavage with 2 x 4 ml washes with harvest solution (0.02% EDTA in PBS). Viable cells were counted from individual

mice from each group. Mice injected with $50 \,\mu g$ of muKS1 had on average a 3-fold increase in cell numbers (Fig. 10).

20 µg of bacterial recombinant muKS1 was injected subcutaneously into the left hind foot of three C3H/HeJ mice. The same volume of PBS was injected into the same site on the right-hand side of the same animal. After 18 hours, mice were examined for inflammation. All mice showed a red swelling in the foot pad injected with bacterially recombinant KS1. From histology, sites injected with muKS1 had an inflammatory response of a mixed phenotype with mononuclear and polymorphonuclear cells present.

Injection of bacterially expressed muKS1a into nude mice

To determine whether T cells are required for the inflammatory response, the experiment was repeated using nude mice. Two nude mice were anaesthetised intraperitoneally with 75 µl of 1/10 dilution of Hypnorm (Janssen Pharmaceuticals, Buckinghamshire, England) in phosphate buffered saline. 20ug of bacterially expressed muKS1a (SEQ ID NO: 345) was injected subcutaneously in the left hind foot, ear and left-hand side of the back. The same volume of phosphate buffered saline was injected in the same sites but on the right-hand side of the same animal. Mice were left for 18 hours and then examined for inflammation. Both mice showed a red swelling in the ear and foot sites injected with the bacterially expressed protein. No obvious inflammation could be identified in either back site. Mice were culled and biopsies taken from the ear, back and foot sites and fixed in 3.7% formol saline. Biopsies were embedded, sectioned and stained with Haemotoxylin and eosin. Sites injected with muKS1a had a marked increase in polymorphonuclear granulocytes, whereas sites injected with phosphate buffered saline had a low background infiltrate of polymorphonuclear granulocytes.

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Discussion

Chemokines are a large superfamily of highly basic secreted proteins with a broad number of functions (Baggiolini, et al., Annu. Rev. Immunol., 15:675-705, 1997; Ward, et al., Immunity, 9:1-11, 1998; Horuk, Nature, 393:524-525, 1998). The polypeptide

sequences of muKS1 and huKS1 have similarity to CXC chemokines, suggesting that this protein will act like other CXC chemokines. The in vivo data from nude mice supports this hypothesis. This chemokine-like protein may therefore be expected to stimulate leukocyte, epithelial, stromal, and neuronal cell migration; promote angiogenesis and vascular development; promote neuronal patterning, hemopoietic stem cell mobilization, keratinocyte and epithelial stem cell patterning and development, activation and proliferation of leukocytes; and promotion of migration in wound healing events. It has recently been shown that receptors to chemokines act as co-receptors for HIV-1 infection of CD4+ cells (Cairns, et al., Nature Medicine, 4:563-568, 1998) and that high circulating levels of chemokines can render a degree of immunity to those exposed to the HIV virus (Zagury, et al., Proc. Natl. Acad. Sci. USA 95:3857-3861, 1998). This novel gene and its encoded protein may thus be usefully employed as regulators of epithelial, lymphoid, myeloid, stromal, and neuronal cells migration and cancers; as agents for the treatment of cancers, neuro-degenerative diseases, inflammatory autoimmune diseases such as psoriasis, asthma and Crohn's disease for use in wound healing; and as agents for the prevention of HIV-1 binding and infection of leukocytes.

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We have also shown that muKS1 promotes a quantifiable increase in cell numbers in the peritoneal cavity of C3H/HeJ mice injected with muKS1. Furthermore, we have shown that muKS1 induces an oxidative burst in human peripheral blood mononuclear cells and migration in the human monocyte leukemia cell line, THP-1, suggesting that monocyte/macrophages are one of the responsive cell types for KS1. In addition to this, we demonstrated that huKS1 was expressed at high levels in a number of non-lymphoid tissues, such as the colon and small intestine, and in breast tumors. It was also expressed in normal uterine and cervical tissue, but was completely down-regulated in their respective tumors. It has recently been shown that non-ELR chemokines have demonstrated angiostatic properties. IP-10 and Mig, two non-ELR chemokines, have previously been shown to be up-regulated during regression of tumors (Tannenbaum CS, Tubbs R, Armstrong D, Finke JH, Bukowski RM, Hamilton TA, "The CXC Chemokines IP-10 and Mig are necessary for IL-12-mediated regression of the mouse RENCA

tumor," *J. Immunol.* 161: 927-932, 1998), with levels of expression inversely correlating with tumor size (Kanegane C, Sgadari C, Kanegane H, Teruya-Feldstine J, Yao O, Gupta G, Farber JM, Liao F, Liu L, Tosato G, "Contribution of the CXC Chemokines IP-10 and Mig to the antitumor effects of IL-12," *J. Leuko. Biol.* 64: 384-392, 1998). Furthermore, neutralizing antibodies to IP-10 and Mig would reduce the anti-tumor effect, indicating the contribution these molecules make to the anti-tumor effects. Therefore, it is expected that in the case of cervical and uterine tumors, KS1 would have similar properties.

The data demonstrates that KS1 is involved in cell migration showing that one of the responsive cell types is monocyte/macrophage. The human expression data in conjunction with the *in vitro* and *in vivo* biology demonstrates that this molecule may be a useful regulator in cell migration, and as an agent for the treatment of inflammatory diseases, such as Crohn's disease, ulcerative colitis, and rheumatoid arthritis; and cancers, such as cervical adenocarcinoma, uterine leiomyoma, and breast invasive ductal carcinoma.

Example 6

CHARACTERIZATION OF KS2

KS2 contains a transmembrane domain and may function as either a membrane-bound ligand or a receptor. Northern analysis indicated that the mRNA for KS2 was expressed in the mouse keratinocyte cell line, Pam212, consistent with the cDNA being identified in mouse keratinocytes.

Mammalian Expression

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To express KS2, the extracellular domain was fused to the amino terminus of the constant domain of immunoglobulinG (Fc) that had a C-terminal 6xHistidine tag. This was performed by cloning polynucleotides 20-664 of KS2 (SEQ ID NO: 273), encoding amino acids 1-215 of polypeptide KS2 (SEQ ID NO: 347), into the mammalian expression vector pcDNA3 (Invitrogen, NV Leek, Netherlands), to the amino terminus of

the constant domain of immunoglobulinG (Fc) that had a C-terminal 6xHistidine tag. This construct was transformed into competent XL1-Blue *E. coli* as described in Sambrook et al., *Ibid.* The Fc fusion construct of KS2a was expressed by transfecting Cos-1 cells in 5 x T175 flasks with 180 µg of KS1a using DEAE-dextran. The supernatant was harvested after seven days and passed over a Ni-NTA column. Bound KS2a was eluted from the column and dialysed against PBS.

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The ability of the Fc fusion polypeptide of KS2a to inhibit the IL-2 induced growth of concanavalin A stimulated murine splenocytes was determined as follows. A single cell suspension was prepared from the spleens of BALB/c mice and washed into DMEM (GIBCO-BRL) supplemented with 2 mM L-glutamine, 1 mM sodium pyruvate, 0.77 mM L-asparagine, 0.2 mM L-arganine, 160 mM penicillin G, 70 mM dihydrostreptomycin sulfate, 5 x 10⁻² mM beta mercaptoethanol and 5% FCS (cDMEM). Splenocytes (4 x 10^6 /ml) were stimulated with 2 μ g/ml concanavalin A for 24 hrs at 37°C in 10% CO₂. The cells were harvested from the culture, washed 3 times in cDMEM and resuspended in cDMEM supplemented with 10 ng/ml rhuIL-2 at 1 x 105 cells/ml. The assay was performed in 96 well round bottomed plates in 0.2 ml cDMEM. The Fc fusion polypeptide of KS2a, PBS, LPS and BSA were titrated into the plates and 1 x 104 activated T cells (0.1 ml) were added to each well. The plates were incubated for 2 days in an atmosphere containing 10% CO₂ at 37°C. The degree of proliferation was determined by pulsing the cells with 0.25 uCi/ml tritiated thymidine for the final 4 hrs of culture after which the cells were harvested onto glass fiber filtermats and the degree of thymidine incorporation determined by standard liquid scintillation techniques. As shown in Fig. 6, the Fc fusion polypeptide of KS2a was found to inhibit the IL-2 induced growth of concanavalin A stimulated murine splenocytes, whereas the negative controls PBS, BSA and LPS did not.

This data demonstrates that KS2 is expressed in skin keratinocytes and inhibits the growth of cytokine induced splenocytes. This indicates a role for KS2 in the regulation of skin inflammation and malignancy.

Example 7

Characterization of KS3

KS3 encodes a polypeptide of 40 amino acids (SEQ ID NO: 129). KS3 contains a signal sequence of 23 amino acids that would result in a mature polypeptide of 17 amino acids (SEQ ID NO: 348; referred to as KS3a).

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KS3a was prepared synthetically (Chiron Technologies, Victoria, Australia) and observed to enhance transferrin-induced growth of the rat intestinal epithelial cells IEC-18 cells. The assay was performed in 96 well flat-bottomed plates in 0.1 ml DMEM (GIBCO-BRL Life Technologies) supplemented with 0.2% FCS. KS3a (SEQ ID NO: 348), apo-Transferrin, media and PBS-BSA were titrated either alone, with 750 ng/ml Apo-transferrin or with 750 ng/ml BSA, into the plates and 1 x10³ IEC-18 cells were added to each well. The plates were incubated for 5 days at 37⁰C in an atmosphere containing 10% CO₂. The degree of cell growth was determined by MTT dye reduction as described previously (*J. Imm. Meth.* 93:157-165, 1986). As shown in Fig. 7, KS3a plus Apo-transferrin was found to enhance transferrin-induced growth of IEC-18 cells, whereas KS3a alone or PBS-BSA did not, indicating that KS3a and Apo-transferrin act synergistically to induce the growth of IEC-18 cells.

This data indicates that KS3 is epithelial derived and stimulates the growth of epithelial cells of the intestine. This suggests a role for KS3 in wound healing, protection from radiation- or drug-induced intestinal disease, and integrity of the epithelium of the intestine.

SEQ ID NOS: 1-725 are set out in the attached Sequence Listing. The codes for polynucleotide and polypeptide sequences used in the attached Sequence Listing confirm to WIPO Standard ST.25 (1988), Appendix 2.

All references cited herein, including patent references and non-patent references, are hereby incorporated by reference in their entireties.

Although the present invention has been described in terms of specific embodiments, changes and modifications can be carried out without departing from the

scope of the invention which is intended to be limited only by the scope of the appended claims.

We claim:

- 1. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of: (a) sequences recited in SEQ ID NOS: 466-487, 510, 511 and 514-623; (b) complements of the sequences recited in SEQ ID NOS: 466-487, 510, 511 and 514-623; (c) reverse complements of the sequences recited in SEQ ID NOS: 466-487, 510, 511 and 514-623; (d) reverse sequences of the sequences recited in SEQ ID NOS: 466-487, 510, 511 and 514-623; (e) sequences having at least a 99% probability of being the same as a sequence selected from any of the sequences in (a)-(d), above, as measured by the computer algorithm BLASTP using the running parameters described above; (f) nucleotide sequences having at least 75% identity to any of the sequences in (a)-(d), above, as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; (g) nucleotide sequences having at least 90% identity to any of the sequences in (a)-(d), above, as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; (h) nucleotide sequences having at least 95% identity to any of the sequences in (a)-(d), above, as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; and (g) open reading frames of SEQ ID NOS: 1-119, 198-276, 349-372, 399-405, 410-412, 416, 418-455, 464, 466-487, 510, 511 and 514-623.
 - 2. An expression vector comprising an isolated polynucleotide of claim 1.
 - 3. A host cell transformed with an expression vector of claim 2.
- 4. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of: (a) sequences provided in SEQ ID NOS: 488-509, 512, 513 and 624-725; (b) sequences having at least a 99% probability of being the same as a sequence of SEQ ID NOS: 488-509, 512, 513 and 624-725, as measured by the computer algorithm BLASTP using the running parameters described above; (c) sequences having

at least 75% identity to a sequence provided in SEQ ID NOS: 488-509, 512, 513 and 624-725, as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; (d) sequences having at least 90% identity to a sequence provided in SEQ ID NOS: 488-509, 512, 513 and 624-725, as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; (e) sequences having at least 95% identity to a sequence provided in SEQ ID NOS: 488-509, 512, 513 and 624-725, as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; and (f) sequences encoded by a sequence provided in SEQ ID NOS: 488-509, 512, 513 and 624-725.

- 5. An isolated polynucleotide encoding a polypeptide of claim 4.
- 6. An expression vector comprising an isolated polynucleotide of claim 5.
- 7. A host cell transformed with an expression vector of claim 6.
- 8. An isolated polypeptide comprising at least a functional portion of a polypeptide having an amino acid sequence selected from the group consisting of: (a) sequences provided in SEQ ID NOS: 196, 488-509, 512, 513 and 624-725; (b) sequences having at least a 99% probability of being the same as a sequence of SEQ ID NOS: 196, 488-509, 512, 513 and 624-725, as measured by the computer algorithm BLASTP using the running parameters described above; (c) sequences having at least 75% identity to a sequence provided in SEQ ID NOS: 196, 488-509, 512, 513 and 624-725, as measured by the computer algorithm BLASTP, using the running parameters and identity test defined above; (d) sequences having at least 90% identity to a sequence provided in SEQ ID NOS: 196, 488-509, 512, 513 and 624-725, as measured by the computer algorithm BLASTP, using the running parameters and identity test defined above; (e) sequences having at least 95% identity to a sequence provided in SEQ ID

NOS: 196, 488-509, 512, 513 and 624-725, as measured by the computer algorithm BLASTP, using the running parameters and identity test defined above; and (f) sequences encoded by a sequence provided in SEQ ID NOS: 466-487, 510, 511 and 514-623.

- 9. A method for stimulating keratinocyte growth and motility in a patient, comprising administering to the patient a composition comprising a polypeptide of claim 4.
- 10. The method of claim 9, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (a) SEQ ID NOS: 187, 196, 342, 343, 395, 397 and 398; (b) sequences having at least about 50% identity to a sequence of SEQ ID NOS: 187, 196, 342, 343, 395, 397 and 398 as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; (c) sequences having at least about 75% identity to a sequence of SEQ ID NOS: 187, 196, 342, 343, 395, 397 and 398 as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; (d) sequences having at least about 90% identity to a sequence of SEQ ID NOS: 187, 196, 342, 343, 395, 397 and 398 as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; and (e) sequences comprising amino acids 54-104 of SEQ ID NO: 196.
- 11. A method for inhibiting the growth of cancer cells in a patient, comprising administering to the patient a composition comprising a polypeptide of claim 4.
- 12. The method of claim 11, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (a) SEQ ID NOS: 187, 196, 342, 343, 397 and 398; (b) sequences having at least 75% identity to a sequence of SEQ ID NOS: 187, 196, 342, 343, 397 and 398, as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; (c) sequences having at least 90%

identity to a sequence of SEQ ID NOS: 187, 196, 342, 343, 397 and 398, as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; (d) sequences having at least 95% identity to a sequence of SEQ ID NOS: 187, 196, 342, 343, 397 and 398, as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; and (e) sequences comprising amino acids 54-104 of SEQ ID NO: 196.

- 13. A method for modulating angiogenesis in a patient, comprising administering to the patient a composition comprising a polypeptide of claim 4.
- 14. The method of claim 13, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (a) SEQ ID NOS: 187, 196, 342, 343, 397 and 398; (b) sequences having at least 75% identity to a sequence of SEQ ID NOS: 187, 196, 342, 343, 397 and 398 as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; (c) sequences having at least 90% identity to a sequence of SEQ ID NOS: 187, 196, 342, 343, 397 and 398 as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; (d) sequences having at least 95% identity to a sequence of SEQ ID NOS: 187, 196, 342, 343, 397 and 398 as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; and (e) sequences comprising amino acids 54-104 of SEQ ID NO: 196..
- 15. A method for inhibiting angiogenesis and vascularization of tumors in a patient, comprising administering to a patient a composition comprising a polypeptide of claim 4.
- 16. The method of claim 15, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (a) SEQ ID NOS: 187, 196, 342, 343, 397 and 398; (b) sequences having at least 75% identity to a sequence of SEQ ID NOS:

187, 196, 340, 342-346, 397 and 398, as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; (c) sequences having at least 90% identity to a sequence of SEQ ID NOS: 187, 196, 340, 342-346, 397 and 398, as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; (d) sequences having at least 95% identity to a sequence of SEQ ID NOS: 187, 196, 340, 342-346, 397 and 398, as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; and (e) sequences comprising amino acids 54-104 of SEQ ID NO: 196.

- 17. A method for modulating skin inflammation in a patient, comprising administering to the patient a composition comprising a polypeptide of claim 4.
- 18. The method of claim 17, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (a) SEQ ID NOS: 338 and 347; and (b) sequences having at least 75% identity to a sequence of SEQ ID NOS: 338 and 347 as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; (c) sequences having at least 90% identity to a sequence of SEQ ID NOS: 338 and 347 as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; and (d) sequences having at least 95% identity to a sequence of SEQ ID NOS: 338 and 347 as measured by the computer algorithm BLASTP using the running parameters and identity test defined above.
- 19. A method for stimulating the growth of epithelial cells in a patient, comprising administering to the patient a composition comprising a polypeptide of claim 4.
- 20. The method of claim 19, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (a) SEQ ID NOS: 129 and 348; (b) sequences having at least 75% identity to a sequence of SEQ ID NOS: 129 and 348 as measured by the computer algorithm BLASTP using the running parameters and identity

test defined above; (c) sequences having at least 90% identity to a sequence of SEQ ID NOS: 129 and 348 as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; and (d) sequences having at least 95% identity to a sequence of SEQ ID NOS: 129 and 348 as measured by the computer algorithm BLASTP using the running parameters and identity test defined above.

- 21. A method for inhibiting the binding of HIV-1 to leukocytes in a patient, comprising administering to the patient a composition comprising a polypeptide of claim 4.
- 22. The method of claim 21, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (a) SEQ ID NOS: 340, 344, 345, 346 and 465; (b) sequences having at least 75% identity to a sequence of SEQ ID NOS: 340, 344, 345, 346 and 465 as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; (c) sequences having at least 90% identity to a sequence of SEQ ID NOS: 340, 344, 345, 346 and 465 as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; and (d) sequences having at least 95% identity to a sequence of SEQ ID NOS: 340, 344, 345, 346 and 465 as measured by the computer algorithm BLASTP using the running parameters and identity test defined above.
- 23. A method for treating an inflammatory disease in a patient, comprising administering to the patient a composition comprising a polypeptide of claim 4.
- 24. The method of claim 23, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (a) SEQ ID NOS: 340, 344, 345, 346 and 465; (b) sequences having at least 75% identity to a sequence of SEQ ID NOS: 340, 344, 345, 346 and 465 as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; (c) sequences having at least 90%

identity to a sequence of SEQ ID NOS: 340, 344, 345, 346 and 465 as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; and (d) sequences having at least 95% identity to a sequence of SEQ ID NOS: 340, 344, 345, 346 and 465 as measured by the computer algorithm BLASTP using the running parameters and identity test defined above.

- 25. A method for treating cancer in a patient, comprising administering to the patient a composition comprising a polypeptide of claim 4.
- 26. The method of claim 25, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (a) SEQ ID NOS: 340, 344, 345, 346 and 465; (b) sequences having at least 75% identity to a sequence of SEQ ID NOS: 340, 344, 345, 346 and 465 as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; (c) sequences having at least 90% identity to a sequence of SEQ ID NOS: 340, 344, 345, 346 and 465 as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; and (d) sequences having at least 95% identity to a sequence of SEQ ID NOS: 340, 344, 345, 346 and 465 as measured by the computer algorithm BLASTP using the running parameters and identity test defined above.
- 27. A method for treating a neurological disease in a patient, comprising administering to the patient a composition comprising a polypeptide of claim 4.
- 28. The method of claim 27, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (a) SEQ ID NOS: 187, 196, 340, 342-346, 397 and 398; (b) sequences having at least 75% identity to a sequence of SEQ ID NOS: 187, 196, 340, 342-346, 397 and 398, as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; (c) sequences having at least 90% identity to a sequence of SEQ ID NOS: 187, 196, 340, 342-346, 397

and 398, as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; (d) sequences having at least 95% identity to a sequence of SEQ ID NOS: 187, 196, 340, 342-346, 397 and 398, as measured by the computer algorithm BLASTP using the running parameters and identity test defined above; and (e) sequences comprising amino acids 54-104 of SEQ ID NO: 196.

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ataagacaaa ttatatattg ctatgaagct cttcttacca gggtcagttt ttacatttta
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960
aa
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<210> 45

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540
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acacaggtga cagtcccaag tagataacct ccatgggaca agttgggtgt tgccttaccc
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geetgeecag ce
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ctaatataga ttatttatga attcaggtgg cttaatggta tatgcatgaa ttagtagtaa
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aacaagaact agggccagca agtggcttaa gggtgcctgc taaccatctc agccacctga
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gcccacagct ccggtcggcc ctgtgccacc caccaacctc ctggatggga tcgtggactt
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cagcgaggtc cctgacaggg cacctgacag ccggcaggaa gagggcctgg acttcttcca
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ccccag
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gagettgecc cacaagtete teggggatgt tgtactettg tgtgtgttta cagtateatg
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gctgttacat ctactggtc
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tctacctcct cctcgggggc ttctccttct gcnaagttcg tctcaataag cgcaaggaat
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     <212> DNA
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     <220>
      <221> unsure
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      <221> unsure
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aagcctgcct cgctgccagc cttgccctag cgctaaatgg tgtctttacc aacatcataa
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tgcccattct t
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egeeggtgee thettetggt tggtgtetet getgettteg tetgttttet ggtteetagt
gagagtcatc actgacaaca gagatggacc agtacagaat tacctgct
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     <210> 54
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     <212> DNA
      <213> Human
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aacaagatca cagetteeta tgaggacegg gtgaeettet tgecaactgg tateacette
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aagtccgtga cacgggaaga cactgggaca tacacttgta tgg
                                                                     403 ·
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     <211> 413
     <212> DNA
     <213> Human
     <400> 55
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<210> 56

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     <210> 57
     <211> 190
     <212> DNA
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     <220>
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cagtgtgcaa catatataaa acagaaatac taactctaca ggcagtatgt cgacgcggcc
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gcgtattcgg
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     <210> 58
     <211> 413
     <212> DNA
     <213> mouse
     <400> 58
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     <210> 59
     <211> 325
     <21.2> DNA
     <213> mouse
     <220>
     <221> unsure
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     <221> unsure
     <222> (223)...(223)
     <221> unsure
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     <221> unsure
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2220

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 gggaaactga aaagcaacct agggacactg taagcagaaa gctgaggctt ttaaaaaccc
                                                                       120
 accttggcaa tgtaacttgg gaggttccca cacacccagg gctgtgcatc gtgaaattct
                                                                       180
 gtctcctgag acgctgagaa acccttcctt gcagctataa tgggcctggc cgcccagtgt
 ggagetgtag cttcccacga cgtagecete aggaacttea ggagggatge cacagtetat
                                                                       300
 ttctgaaaac aaaaccgtgt caacttcttt actttacaaa tgcaagtttt cagaatccac
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 catctctctg cacccatacc ccatgcctca caccccagac cctgtgttag
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<220>

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                                                                120
agaagagttt atgggaaatc ttggagaaaa cattggatgg tttgagagaa tggttaggag
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     <212> DNA
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                                                                120
actettagae atgggtgtge teactgaact etagggtetg tgtgctagat getgccaacg
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ctgtattcag gacctgaagt gagtacccgt gtggatccag accaatccag tgtgagacta
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ctgaagaaca tctgttgcca gaacggccac accaaacaga tggagtgccc cagcacttag
                                                                300
cttcttaaat aacatcggaa ccattcagcc agcgagtctg tgtttgcttt ttgttaaatt
                                                                360
gtccgccgaa tctaaattcc tccaaaaggc ttgtgacc
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                                                                120
gttcgaggaa gcccggctgg accatagtgg ccacggcggt gaggtaggcg tggacagggc
                                                                180
tgaccagtcc aagttaagga cgttcgggtc catgttaacc ctgccttgta cgtccagcat
                                                                240
cgtaagaaaa aacacttgag aacccgaaga ggagatgga
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                                                                 * 45%
60
                                                                120
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                                                                180
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                                                                240
attaaaacgg gactttacaa gcattctaga agactcaaac ttgaagcaat ttttggaaaa
                                                                300
taaatgtaca gagaaaagat cttgaagcta ctgaacagag aaccctcatt aaccgagcaa
                                                                360
atacatccta tggagcttcc gaggagtaca cagacagacc g
                                                                401
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     <212> DNA
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                                                                          120
 tgagcaattt cgggatatgc cctaccagcc attcagcaaa ggagatcggc tgggaaaggt
                                                                          180
                                                                         240
 tgcagactgg acaggggcca cataccagga caagaggtac acaaacaagt attcctctca
gttcggtggg gggagtcagt atgcatattt ccatgaggag gatgagacaa gctttccagc
                                                                          300
                                                                          307
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                                                                         120
tgggaaccag acagcettge tteactgtat aagtgeeetg atcacacgea gaatgaagtg ceaggttget cagaageaca aagggtgtgg ctactggeee taaccatgga ctacgtggtt
                                                                         180
                                                                         240
ctaaccaaag actctagaac tctggggtgg gggagaaaca atgtgttctg tgctccagaa
                                                                         300
cettnggett cetggeecat atggatggge ttggeaagga acctacetet tetetaaggt
                                                                         360
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 gggtggggtg ggagggggg gagccaccgc taccgccgcc gcctcccggg tgggcgccct
                                                                          120
 tctccttaga cgccggcgac ccaggacgag ggcttcatca ctgtaaatgg ttgcaagccg
                                                                          180
 acaaagctgc acctcctgaa aaagacggac agcccatcgc gtgagctgta gaaatttgtg
                                                                          240
                                                                          257
 gacgcatttc tatcggt
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                                                    _ ,
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                                                                          120
 cagceettee tgteaagtee etagcacage gggaggcaga gtatgeagag geteggagae
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ggagcaagaa tgagcttagg ttgggaggga atggggcgtg ggggagctgg agcaagacca
                                                                     180
eggeetggtg geageeggte geeetaeagg ecceattece geetggeact gteeteetta
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cageggaaac acagagettg tgagtgcatg teagetgtta acaagtggtt tetagtacat
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                                                                     120
gccatggaga tcctcaaagt gctctttaat atcacctttg actctgtcaa gagggaagtt
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gatgaggaag atgctgccct ttaccggtac ctggggactc ttctgcggca ctgcgtgatg
                                                                     240
gttgaagetg etggggaeeg cacagaggag ttecaeggee acaeggtgaa teteetgggg
                                                                     300
aacttgcccc tcaagtgttt ggatgtgctt ctggccctgg agctccacga aggatcctta
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gagtcaatgg
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tectacettg cetgtettet eteteetggg aagatgttee tggtgggget gaegggagge
ategecteag geaagagete egteateeag gtatteeaac agetgggetg tgetgtaate
                                                                     180
gacgtggacg tcattgcgcg gcacgttgtc cagccagggt atcctgccca ccggcgtata
                                                                     240
gtagaggcct ttggcactga agtcttgctg gagaatggcg acatcgaccg caaggtcctc
                                                                     300
ggagacetga tetteaacea geetgacegt eggeagetge teaactecat tacceaceet
                                                                     360
gagateegea aggaaatgat gaaggagace ttcaagtact teteegaggt accgatacgt
                                                                      420
                                                                     423
gat
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gcccgcgtcg gtgactgggg tctcacacag gttcagcact tggagcatag tgaggtg
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     <213> mouse
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cagctctggt ctg
                                                                     133
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tttcttctcc aggctgaaga cctgaacgtc aagttggaag gggagccttc catgcggaaa
                                                                     120
ccaaagcagc ggccgcggcc ggagcccctc ancancccca ccaangeggg cactttcatc
                                                                     180
gcccctcctg tctactccaa catcacccct taccaga
                                                                     217
     <210> 108
     <211> 346
     <212> DNA
     <213> mouse
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gggcatagaa ggcatctcga aaagaatact tatttgaatt gaaggaagat gaagaggcot gcaggaaggc tcagaagaca ggagtgtttt acctctttca tgacctggat cctttgctcc aggcgtcagg acatcgatac ctggtgcccc ggcttagccg agcagagttg gaagggctgc tgggtaagtt cggacaggat tcgcaaagaa ttgaagattc ggtgctggtt gggtgctccg agcagcagga agcatggttt gctttggatc taggtctgaa gagtgcctcc tccagccgtg gacaagtatc gctgctccag cagcttgact gctgtaaaga ggatct	60 120 180 240 300 346
<210> 109 <211> 242 <212> DNA <213> mouse	
<pre><400> 109 ccacattgtc cacaactgga aggcacgatg gttcatcctt cggcagaaca cgctcctgta ttacaagcta gagggtggcc ggcgagtaac cccgcccaag gggaggattg tccttgatgg ctgcaccatc acctgcccct gcctggagta tgaaaaccgg ccgctcctca ttaaactgaa gacccgaact tccactgagt acttcctgga agcctgttct cgagaggaga gagactcctg gg</pre>	60 120 180 240 242
<210> 110 <211> 310 <212> DNA <213> mouse	
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<210> 111 <211> 228 <212> DNA <213> mouse	ď
<400> 111 ttcttttta acatttggtg gtttttttct ttactctttt tttcttttcc ttcttttct gccctcaacc ccccaactcc tttggtatga agtactttta acatttatat ttcattgtta cactttaaat tttgtaagga aaactctgat attcattcc tcctgaacca ctaatgttag aatttatttc taagaatcag tcaacatgta tactcttaat agtgaatt	60 120 180 228
<210> 112 <211> 292 <212> DNA <213> mouse	
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	cgctatagtg cccaggtgac					240 292
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caaccagaaa actacaagaa	taggacttta aagacctcag cagccacgtg gcctaaccga	caatgtatag atcacagttt	acctggaata gagggtggaa	tatagtgttg ggcaggggtg	ccctggttaa tgactgagtt	60 120 180 240 255
<211: <212:	> 114 > 197 > DNA > mouse					
gacccacatg tgcatgtgcg	> 114 tgaacagccg ctcttggtct gttttattcc tacagat	ttccacttat	tgcctcgttc	gtaagaaacc	aaccataagg	60 120 180 197
<211: <212:	> 115 > 205 > DNA > mouse				,	
aaaacatttc aacataggtg gtcatataca	> 115 acaaaacagc aaaacagcca tggtatatac gttatagaca	aacacataat atatatactt	gtacaatctg	gtgttccagg	acaaacatct	60 120 180 205
<211: <212:	> 116 > 202 > DNA > mouse				e.	. 45
<220	>			.,		
cctccctcat tgcacacaca cacacacaca	> 116 cetetaette cacacacaca ctgtecatec gtcagtgeet	cacacacaca atagttactt	cacgaacaca	cgcacacaca	cacacacacg	60 120 180 202
<211 <212	> 117 > 240 > DNA > mouse			·		

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cgcttctgct gtgtgaagga gcgcaagccc tggagtgcta cagctgcgtg cagaaggcgg
                                                                 120
                                                                 180
acgatggatg cgctccgcac aggatgaaga cagtcaaatg tggtcccggg gtggacgtct
gtaccgaggc cgtgggagcg gtagagacca tccacgggca attctctgtg gcggtgcggg
                                                                 240
     <210> 118
     <211> 527
     <212> DNA
     <213> Human
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gttccaatat cagtctatct tttattcaac gcaatgacag cactgaccga agaggcagcc
                                                                 120
gtgactgtaa cacctccaat cacagcccag caaggtaact ggacagttaa caaaacagaa
                                                                 180
gctcacaaca tagaaggacc catagccttg aagttctcac acctttgcct ggaagatcat
                                                                 240
aacagttact gcatcaacgg tgcttgtgca ttccaccatg agctagagaa agccatctgc
                                                                 300
aggtgtttta ctggttatac tggagaaagg tgtgagcact tgactttaac ttcatatgct
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gtggattctt atgaaaaata cattgcaatt gggattggtg ttggattact attaagtggt
                                                                 420
tttcttgtta ttttttactg ctatataaga aagaggtgtc taaaattgaa atcgccttac
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     <213> Rat
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                                                                 120
ccccagtac ggctcttcac cgaggaggag ctggcccgct acagcggcga ggaggaggat
                                                                 180
                                                                 240
caacccatct acttggcagt gaagggagtg gtgttcgatg tcacctctgg gaaggagttt
tatggacgtg gagcccccta caacgccttg gccgggaagg actcgagcag aggtgtggcc
                                                                 300
aagatgtege tggateetge agaceteact catgacattt etggteteac tgecaaggag
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ctggaagccc tcgatgacat cttcagcaag gtgtacaaag ccaaataccc cattgttggc
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tacacqqccc qcaggatcct caacqaggat ggcagcccca acctggactt caagcctgaa
                                                                 480
gaccagcccc attttgacat aaaggacgag ttctaatgtc tagctgagaa gctggttcta
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gggagaggtg aggggacagg agttaaatgt cccacggaac aagcagggga agcctctgag
                                                                 600
655
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     <211> 176
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                                                                   2.425
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            5 10 15
1
Pro Val Val Ala Tyr Ser Val Ser Leu Pro Ala Ser Phe Leu Glu Glu
        20 25 30
Val Ala Gly Ser Gly Glu Ala Glu Gly Ser Ser Ala Ser Ser Pro Ser
       35
                        40
                                         . 45
Leu Leu Pro Pro Arg Thr Pro Ala Phe Ser Pro Thr Pro Gly Arg Thr
   50
                    55 60
Gln Pro Thr Ala Pro Val Gly Pro Val Pro Pro Thr Asn Leu Leu Asp
                  70
                           ,
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Gly Ile Val Asp Phe Phe Arg Gln Tyr Val Met Leu Ile Ala Val Val
         85 90 95
Gly Ser Leu Thr Phe Leu Ile Met Phe Ile Val Cys Ala Ala Leu Ile
      100 105 110
Thr Arg Gln Lys His Lys Ala Thr Ala Tyr Tyr Pro Ser Ser Phe Pro
115 120 125
Glu Lys Lys Tyr Val Asp Gln Arg Asp Arg Ala Gly Gly Pro His Ala
130 135 140
Leu Asp Phe Phe Gln Gln Leu Gln Ala Asp Ile Leu Ala Cys Tyr Ser
   165 170
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    <213> Rat
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Ser Arg Thr Gln Lys Leu Pro Thr Arg Asp Glu Glu Leu Phe Gln Met
 20 25 30
Gln Ile Arg Asp Lys Ala Leu Phe His Asp Ser Ser Val Ile Pro Asp
 35 40
                                45
Gly Ala Glu Ile Ser Ser Tyr Leu Phe Arg Asp Thr Pro Arg Arg Tyr
 50 55
                       60
Phe Phe Met Val Glu Glu Asp Asn Thr Pro Leu Ser Val Thr Val Thr 65 70 75 80
Pro Cys Asp Ala Pro Leu Glu Trp Lys Leu Ser Leu Gln Glu Leu Pro
        85 90 95
Glu Glu Ser Ser Ala Asp Gly Ser Gly Asp Pro Glu Pro Leu Asp Gln
      100 105
Gln Lys Gln Gln
  115
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Ser Asp Gly Asp Thr Thr Ala Ser Pro Ser Ser Met Ser Ser Ser Ser
     20 25 30 .
Val Leu Asn His Ile Ser Ser Ser Ser Ser Val Trp His Leu Phe
   35 40 45
Asp Ile Cys Asp Ser Ser Lys Trp Asn Ala Tyr Cys Gln Val Trp Gly
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Arg Lys Met Leu Pro Thr Gln Phe Leu Phe Leu Gly Val Leu Gly
  20
                           25 30
Ile Phe Gly Leu Thr Phe Ala Phe Ile Ile Gly Leu Asp Gly Ser Thr
  35
                       40 .
                                          45
Gly Pro Thr Arg Phe Phe Leu Phe Gly Ile Leu Phe Ser Ile Cys Phe
  50 55`
Ser Cys Leu Leu
65
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     <211> 110
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Leu Phe Phe Gln Val Ala Pro Leu Ser Val Val Ala Lys Ser Cys Pro 20 25 30
Ser Val Cys Arg Cys Asp Ala Gly Phe Ile Tyr Cys Asn Asp Arg Ser
 35 40
                                            45
Leu Thr Ser Ile Pro Val Gly Ile Pro Glu Asp Ala Thr Thr Leu Tyr
  50
                    55.
Leu Gln Asn Asn Gln Ile Asn Asn Val Gly Ile Pro Ser Asp Leu Lys 65 70 ' 75 75 80
Asn Leu Lys Val Gln Arg Ile Tyr Leu Tyr His Asn Ser Leu Asp
85 90 95
Glu Phe Pro Thr Asn Leu Pro Lys Tyr Val Lys Glu Leu His
   100 105 110
     <210> 125
     <211> 330
     <212> PRT
     <213> mouse
     <400> 125
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Leu Ile Gly Leu Ala Val Ser Ala Arg Val Ala Cys Pro Cys Leu Arg
 20 25 30
Ser Trp Thr Ser His Cys Leu Leu Ala Tyr Arg Val Asp Lys Arg Phe
       35
                       40
Ala Gly Leu Gln Trp Gly Trp Phe Pro Leu Leu Val Arg Lys Ser Lys 50 55 60
Ser Pro Pro Lys Phe Glu Asp Tyr Trp Arg His Arg Thr Pro Ala Ser 65 70 75 80
Phe Gln Arg Lys Leu Leu Gly Ser Pro Ser Leu Ser Glu Glu Ser His
Arg Ile Ser Ile Pro Ser Ser Ala Ile Ser His Arg Gly Gln Arg Thr 100 105 110
Lys Arg Ala Gln Pro Ser Ala Ala Glu Gly Arg Glu His Leu Pro Glu
115 120 125
Ala Gly Ser Gln Lys Cys Gly Gly Pro Glu Phe Ser Phe Asp Leu Leu
130 135 140
```

Pro Glu Val Gln Ala Val Arg Val Thr Ile Pro Ala Gly Pro Lys Ala

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150
                                 155
Ser Val Arg Leu Cys Tyr Gln Trp Ala Leu Glu Cys Glu Asp Leu Ser
165 170 175
Ser Pro Phe Asp Thr Gln Lys Ile Val Ser Gly Gly His Thr Val Asp
        180 . 185 190
Leu Pro Tyr Glu Phe Leu Leu Pro Cys Met Cys Ile Glu Ala Ser Tyr
195 200 205

Leu Gln Glu Asp Thr Val Arg Arg Lys Lys Cys Pro Phe Gln Ser Trp
210 215 220
Pro Glu Ala Tyr Gly Ser Asp Phe Trp Gln Ser Ile Arg Phe Thr Asp
225 230 235
Tyr Ser Gln His Asn Gln Met Val Met Ala Leu Thr Leu Arg Cys Pro
            245 250 255
Leu Lys Leu Glu Ala Ser Leu Cys Trp Arg Gln Asp Pro Leu Thr Pro
260 265 270
Cys Glu Thr Leu Pro Asn Ala Thr Ala Gln Glu Ser Glu Gly Trp Tyr 275 280 285
Ile Leu Glu Asn Val Asp Leu His Pro Gln Leu Cys Phe Lys Phe Ser
 290 295 300
Phe Glu Asn Ser Ser His Val Glu Cys Pro His Gln Ser Gly Ser Leu
305 310 315 320
Pro Ser Trp Thr Val Ser Met Asp Thr Gln
          325 330
    <210> 126
     <211> 37
     <212> PRT
     <213> Rat
    <400> 126
Met Leu Trp Val Leu Leu Ser Leu Thr Pro Leu Leu Ser Pro Leu Ile
             5
                           10
                                             15
Phe Phe Pro Val Lys Thr Val Ala Leu Glu Glu Ile Ser Thr Ile Cys
  20 25
Arg Ala Asp Val Leu
    35
    <210> 127
    <211> 42
     <212> PRT
     <213> mouse
    <400> 127
Met Gly Ser Pro Ile Ser Gly Val Cys Pro Val Leu Pro Gly Gly Leu 1 5 10 15
Phe Val Ala Leu Gly Trp Ile Phe Leu Leu Phe His Arg Asp Ala Phe
    20 25 30
Ser Leu His Thr Met Ser Ala Gly Phe Pro
     35 40
     <210> 128
     <211> 253
     <212> PRT
     <213> mouse
    <400> 128
Met Met Tyr Trp Ile Val Phe Ala Ile Phe Met Ala Ala Glu Thr Phe
```

```
10
                                                  15
              5
Thr Asp Ile Phe Ile Ser Trp Ser Gly Pro Arg Ile Gly Arg Pro Trp 20 25 30
Gly Trp Glu Gly Pro His His His His His Leu Ala Ser Gly Ser His
    35 ·
                     40
                                          45
Lys Pro Leu Pro Leu Leu Thr His Arg Phe Pro Phe Tyr Tyr Glu Phe
 50 55
Lys Met Ala Phe Val Leu Trè Leu Leu Ser Pro Tyr Thr Lys Gly Ala 65 70 75 80
Ser Leu Leu Tyr Arg Lys Phe Val His Pro Ser Leu Ser Arg His Glu 85 90 95
Lys Glu Ile Asp Ala Cys Ile Val Gln Ala Lys Glu Arg Ser Tyr Glu 100 105 110
Thr Met Leu Ser Phe Gly Lys Arg Ser Leu Asn Ile Ala Ala Ser Ala 115 120 125
Ala Val Gln Ala Ala Thr Lys Ser Gln Gly Ala Leu Ala Gly Arg Leu 130 \phantom{\bigg|} 135 \phantom{\bigg|} 140
Arg Ser Phe Ser Met Gln Asp Leu Arg Ser Ile Pro Asp Thr Pro Val
145 150 155 160
Pro Thr Tyr Gln Asp Pro Leu Tyr Leu Glu Asp Gln Val Pro Arg Arg
165 170 175
Arg Pro Pro Ile Gly Tyr Arg Pro Gly Gly Leu Gln Gly Ser Asp Thr
180 185 190
Glu Asp Glu Cys Trp Ser Asp Asn Glu Ile Val Pro Gln Pro Pro Val
 195 200 . 205
Arg Pro Arg Glu Lys Pro Leu Gly Arg Ser Gln Ser Leu Arg Val Val 210 215 220
Lys Arg Lys Pro Leu Thr Arg Glu Gly Thr Ser Arg Ser Leu Lys Val
225 230 235
Arg Thr Arg Lys Lys Ala Met Pro Ser Asp Met Asp Ser
                                250
    245
    <210> 129
    <211> 40
     <212> PRT
     <213> mouse
    <400> 129
Met Lys Ala Met Ala Leu Ser Leu Gly Ala Ser Pro Val Leu Ala Phe
1 5 10 15
Leu Leu Ser Gly Tyr Ser Asp Gly Tyr Gln Val Cys Ser Arg Phe Gly
  20 . 25
Ser Lys Val Pro Gln Phe Leu Asn
      35
     <210> 130
     <211> 87
     <212> PRT
     <213> mouse
     <400> 130
Met Ile Ala Val Thr Phe Ala Ile Val Leu Gly Val Ile Ile Tyr Arg
           5 10
1
                                        . 15
Ile Ser Thr Ala Ala Ala Leu Ala Met Asn Ser Ser Pro Ser Val Arg
    20
                          25
Ser Asn Ile Arg Val Thr Val Thr Ala Thr Ala Val Ile Ile Asn Leu
```

40 ,

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Val Val Ile Ile Leu Leu Asp Glu Val Tyr Gly Cys Ile Ala Arg Trp
50 55
                        60
Leu Thr Lys Ile Gly Glu Cys His Val Gln Asp Ser Ile Gly Ser Met
65 70
                             75
Gly Leu Gly Gln Gly Gln Pro
    <210> 131
    <211> 70
    <212> PRT
    <213> mouse
    <400> 131
Met Phe Gly Leu Val His Val Cys Thr Cys Val Cys Val Cys Val Cys 1 5 10 15
Val Cys Val Cys Val Cys Ile Cys Ser Cys Gly Tyr Val His Val Pro
    20
                        25
                                    30
Cys Gly Cys Val Cys Leu Trp Gly Pro Glu Val Arg Tyr Leu Pro Leu 35
                     40
                                      45
Ser Leu His Pro Gly Gly Phe Cys Phe Val Leu Phe Cys Phe Gly Pro 50 55
Gly Leu Ser Leu Ile Ser
65
    <210> 132
    <211> 63
    <212> PRT
    <213> mouse
  ` <400> 132
Met Trp Leu Val Ala Leu Thr Leu Ser Val Tyr Ser Leu Val Ala
          5
                           10
                                           1.5
Phe Val Thr Gly Met Leu Cys Asp Thr Val Val Ile Lys Met Leu Met 20 25 30
Ser Leu His Lys Ser Ser Lys Leu Asn Pro Arg Ala Lys Cys Gly Gly
35 40
Val Pro Leu Ile Pro Ala Leu Trp Gly Gln Val Gln Val Val Leu
- 50 55
                                    60
    <210> 133
    <211> 39
    <212> PRT
    <213> mouse
    <400> 133
Ile Ser Val Leu Asp Ser Gln Leu Ser Thr Arg Cys Leu Trp Trp Phe
  20
                          25
Ser Lys Asp Leu Glu Val Thr
      35
     <210> 134
     <211> 90
     <212> PRT
     <213> Rat
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<400> 134

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Met Pro Thr Met Trp Pro Leu Leu His Val Leu Trp Leu Ala Leu Val 1 5 10 10 15
Cys Gly Ser Val His Thr Thr Leu Ser Lys Ser Asp Ala Lys Lys Ala
 20 25 30
Ala Ser Lys Thr Leu Leu Glu Lys Thr Gln Phe Ser Asp Lys Pro Val
Gln Asp Arg Gly Leu Val Val Thr Asp Ile Lys Ala Glu Asp Val Val 50 60
Leu Glu His Arg Ser Tyr Cys Ser Ala Arg Ala Arg Glu Arg Asn Phe 65 70 75 80
Ala Gly Glu Val Leu Gly Ile Cys His Ser
     <210> 135
     <211> 193
     <212> PRT
     <213> Rat
    <400> 135
Met Thr Ser Gly Pro Gly Gly Pro Ala Ala Ala Thr Gly Gly Gly Lys
1 10 15
Asp Thr His Gln Trp Tyr Val Cys Asn Arg Glu Lys Leu Cys Glu Ser
20 25 30
Leu Gln Ser Val Phe Val Gln Ser Tyr Leu Asp Gln Gly Thr Gln Ile
 35
           40
                                45
Phe Leu Asn Asn Ser Ile Glu Lys Ser Gly Trp Leu Phe Ile Gln Leu 50 60
Tyr His Ser Phe Val Ser Ser Val Phe Thr Leu Phe Met Ser Arg Thr
65 70 75
Ser Ile Asn Gly Leu Leu Gly Arg Gly Ser Met Phe Val Phe Ser Pro
             85
                               90
Asp Gln Phe Gln Arg Leu Leu Lys Ile Asn Pro Asp Trp Lys Thr His
100 105 110
Arg Leu Leu Asp Leu Gly Ala Gly Asp Gly Glu Val Thr Lys Ile Met 115 120 125
Ser Pro His Phe Glu Glu Ile Tyr Ala Thr Glu Leu Ser Glu Thr Met
                  1.35
                          140
Ile Trp Gln Leu Gln Lys Lys Lys Tyr Arg Val Leu Gly Ile Asn Glu 145 150 155 160
Trp Gln Asn Thr Gly Phe Gln Tyr Asp Val Ile Ser Cys Leu Asn Leu
        165 170 175
Leu Asp Arg Cys Asp Gln Pro Leu Thr Leu Leu Lys Asp Ile Arg Met
          180 185
                                  190
Ser
     <210> 136
     <211> 106
     <212> PRT
     <213> Rat
    <400> 136
Met Ala Ala Pro Met Asp Arg Thr His Gly Gly Arg Ala Ala Arg Ala
1 5 10 15
Leu Arg Arg Ala Leu Ala Leu Ala Ser Leu Ala Gly Leu Leu Ser
        20
                           25
```

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Gly Leu Ala Gly Ala Leu Pro Thr Leu Gly Pro Gly Trp Arg Arg Gln
 35 40 45
Asn Pro Glu Pro Pro Ala Ser Arg Thr Arg Ser Leu Leu Leu Asp Ala
 50 55
                            60
Ala Ser Gly Gln Leu Arg Leu Glu Tyr Gly Phe His Pro Asp Ala Val
              70
                              75
Ala Trp Ala Asn Leu Thr Asn Ala Ile Arg Glu Thr Gly Trp Ala Tyr 85 ' 90 95
Leu Asp Leu Gly Thr Asn Gly Ser Tyr Lys
      100
    <210> 137
    <211> 286
     <212> PRT
    <213> Rat
    <400> 137
Met Ala Ala Ala Met Pro Leu Gly Leu Ser Leu Leu Leu Val Leu
              5
                      10
Val Gly Gln Gly Cys Cys Gly Arg Val Glu Gly Pro Arg Asp Ser Leu
20 25 30
Arg Glu Glu Leu Val Ile Thr Pro Leu Pro Ser Gly Asp Val Ala Ala
 35 40 45
Thr Phe Gln Phe Arg Thr Arg Trp Asp Ser Asp Leu Gln Arg Glu Gly
  50
                 55
Val Ser His Tyr Arg Leu Phe Pro Lys Ala Leu Gly Gln Leu Ile Ser 65 70 75 80
Lys Tyr Ser Leu Arg Glu Leu His Leu Ser Phe Thr Gln Gly Phe Trp 85 90 95
Arg Thr Arg Tyr Trp Gly Pro Pro Phe Leu Gln Ala Pro Ser Gly Ala 100 105 110
Glu Leu Trp Val Trp Phe Gln Asp Thr Val Thr Asp Val Asp Lys Ser
 115 120 125
Trp Lys Glu Leu Ser Asn Val Leu Ser Gly Ile Phe Cys Ala Ser Leu 130 135 140
Asn Phe Ile Asp Ser Thr Asn Thr Val Thr Pro Thr Ala Ser Phe Lys
145 150 155 160
Pro Leu Gly Leu Ala Asn Asp Thr Asp His Tyr Phe Leu Arg Tyr Ala 165 170 175
Val Leu Pro Arg Glu Val Val Cys Thr Glu Asn Leu Thr Pro Trp Lys
180 185 190
Lys Leu Leu Pro Cys Ser Ser Lys Ala Gly Leu Ser Val Leu Leu Lys 195 200 205
Ala Asp Arg Leu Phe His Thr Ser Tyr His Ser Gln Ala Val His Ile
 210 215 220
Arg Pro Ile Cys Arg Asn Ala His Cys Thr Ser Ile Ser Trp Glu Leu
225 230 235 240
Arg Gln Thr Leu Ser Val Val Phe Asp Ala Phe Ile Thr Gly Gln Gly
            245 250 255
Lys Lys Glu Ala Cys Pro Leu Ala Ser Gln Ser Leu Val Tyr Val Asp
      260 265 270
Ile Thr Gly Tyr Ser Gln Asp Asn Glu Thr Leu Glu Val Ser
                280
     <210> 138
     <211> 198
     <212> PRT
```

<213> Rat

<400> 138 Met Thr Val Phe Arg Lys Val Thr Thr Met Ile Ser Trp Met Leu Leu 10 Ala Cys Ala Leu Pro Cys Ala Ala Asp Pro Met Leu Gly Ala Phe Ala 20 25 Arg Arg Asp Phe Gln Lys Gly Gly Pro Gln Leu Val Cys Ser Leu Pro 35 40 Gly Pro Gln Gly Pro Pro Gly Pro Gly Ala Pro Gly Ser Ser Gly 50 55 60 Met Val Gly Arg Met Gly Phe Pro Gly Lys Asp Gly Gln Asp Gly Gln 70 75 Asp Gly Asp Arg Gly Asp Ser Gly Glu Glu Gly Pro Pro Gly Arg Thr 85 90 85 Gly Asn Arg Gly Lys Gln Gly Pro Lys Gly Lys Ala Gly Ala Ile Gly
100 105 110 Arg Ala Gly Pro Arg Gly Pro Lys Gly Val Ser Gly Thr Pro Gly Lys 115 120 125 His Gly Ile Pro Gly Lys Lys Gly Pro Lys Gly Lys Lys Gly Glu Pro 130 135 Gly Leu Pro Gly Pro Cys Ser Cys Gly Ser Ser Arg Ala Lys Ser Ala 145 $$ 150 $$ 155 $$ 160 Phe Ser Val Ala Val Thr Lys Ser Tyr Pro Arg Glu Arg Leu Pro Ile 165 170 175 Lys Phe Asp Lys Ile Leu Met Asn Glu Gly Gly His Tyr Asn Ala Ser 180 Ser Gly Lys Phe Val Cys 195 <210> 139 <211> 233 <212> PRT <213> Rat <400> 139 Met Ala Ser Ala Leu Glu Glu Leu Gln Lys Asp Leu Glu Glu Val Lys ' 10 Val Leu Leu Glu Lys Ser Thr Arg Lys Arg Leu Arg Asp Thr Leu Thr 20 25 30 Lys Ser Gln Lys Lys Pro Glu Phe Asp Asn Glu Lys Pro Ala Ala Val 50 55 60 Val Ala Pro Leu Thr Thr Gly Tyr Thr Val Lys Ile Ser Asn Tyr Gly 65 70 75 80 Trp Asp Gln Ser Asp Lys Phe Val Lys Ile Tyr Ile Thr Leu Thr Gly 85 90 95 Val His Gln Val Pro Ala Glu Asn Val Gln Val His Phe Thr Glu Arg 100 105 110 Ser Phe Asp Leu Leu Val Lys Asn Leu Asn Gly Lys Asn Tyr Ser Met 115. \$120\$

Ile Val Asn Asn Leu Leu Lys Pro Ile Ser Val Glu Ser Ser Ser Lys

130 135 140

165

170

```
Lys Glu Lys Pro Ser Tyr Asp Thr Glu Ala Asp Pro Ser Glu Gly Leu 180 \, 180 \, 180 \, 180 \, 180 \, 181 \, 185 \, 180 \, 190 \, 190 \,
Met Asn Val Leu Lys Lys Ile Tyr Glu Asp Gly Asp Asp Asp Met Lys
    195 200 205
Arg Thr Ile Asn Lys Ala Trp Val Glu Ser Arg Glu Lys Gln Ala Arg
210 215 220
Glu Asp Thr Glu Phe Leu Gln Pro Gly
225 230
     <210> 140
     <211> 38
     <212> PRT
     <213> Human
     <400> 140
Met Gly Leu Ala Leu Cys Leu Ala Ser Ala Gly Ile Ser Gly Ser Arg
1 5
                        10
Ser Ala Phe Leu Gly Val Pro Arg Pro Arg Pro Thr Leu Ile Lys Leu
    20
                         25
Ile Asp Thr Val Asp Leu
       35
      <210> 141
     <211> 322
      <212> PRT
     <213> mouse
     <400> 141
Met Asp Ala Arg Trp Trp Ala Val Val Leu Ala Thr Leu Pro Ser
                                10
Leu Gly Ala Gly Gly Glu Ser Pro Glu Ala Pro Pro Gln Ser Trp Thr 20 25 30
Gln Leu Trp Leu Phe Arg Phe Leu Leu Asn Val Ala Gly Tyr Ala Ser 35 40 45
Phe Met Val Pro Gly Tyr Leu Leu Val Gln Tyr Leu Arg Arg Lys Asn
50 60
Tyr Leu Glu Thr Gly Arg Gly Leu Cys Phe Pro Leu Val Lys Ala Cys 65 70 75 80
Val Phe Gly Asn Glu Pro Lys Ala Pro Asp Glu Val Leu Leu Ala Pro
85 90 95
Arg Thr Glu Thr Ala Glu Ser Thr Pro Ser Trp Gln Val Leu Lyş Leu 100 $105$
Val Phe Cys Ala Ser Gly Leu Gln Val Ser Tyr Leu Thr Trp Gly Ile
115 120 125
Leu Gln Glu Arg Val Met Thr Gly Ser Tyr Gly Ala Thr Ala Thr Ser
130 140 ..
Pro Gly Glu His Phe Thr Asp Ser Gln Phe Leu Val Leu Met Asn Arg
145 150 155 160
Val Leu Ala Leu Val Val Ala Gly Leu Tyr Cys Val Leu Arg Lys Gln
165 170 175
Pro Arg His Gly Ala Pro Met Tyr Arg Tyr Ser Phe Ala Ser Leu Ser
180 185 . 190
Asn Val Leu Ser Ser Trp Cys Gln Tyr Glu Ala Leu Lys Phe Val Ser
     195 200 205
Phe Pro Thr Gln Val Leu Ala Lys Ala Ser Lys Val Ile Pro Val Met
                       215 220
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Met Met Gly Lys Leu Val Ser Arg Arg Ser Tyr Glu His Trp Glu Tyr
225 230 235
Leu Thr Ala Gly Leu Ile Ser Ile Gly Val Ser Met Phe Leu Leu Ser
             245 250
Ser Gly Pro Glu Pro Arg Ser Ser Pro Ala Thr Thr Leu Ser Gly Leu
        260 265 270
Val Leu Leu Ala Gly Tyr Ile Ala Phe Asp Ser Phe Thr Ser Asn Trp
 275 280 285
Gln Asp Ala Leu Phe Ala Tyr Lys Met Ser Ser Val Gln Met Met Phe
290 295 300
Gly Val Asn Leu Phe Ser Cys Leu Phe Thr Val Gly Ser Leu Leu Glu
305 310
                        315
Gln Gly
    <210> 142
    <211> 312
     <212> PRT
    <213> mouse
    <400> 142
Met Leu Cys Leu Cys Leu Tyr Val Pro Ile Ala Gly Ala Ala Gln Thr
         5
                     10 15
Glu Phe Gln Tyr Phe Glu Ser Lys Gly Leu Pro Ala Glu Leu Lys Ser
      20
                        25
                                        30
Ile Phe Lys Leu Ser Val Phe Ile Pro Ser Gln Glu Phe Ser Thr Tyr
 35 40
Arg Gln Trp Lys Gln Lys Ile Val Gln Ala Gly Asp Lys Asp Leu Asp 50 55 60
Gly Gln Leu Asp Phe Glu Glu Phe Val His Tyr Leu Gln Asp His Glu 65 70 75 80
Lys Lys Leu Arg Leu Val Phe Lys Ser Leu Asp Lys Lys Asn Asp Gly
                   90 95
            85
Arg Ile Asp Ala Gln Glu Ile Met Gln Ser Leu Arg Asp Leu Gly Val
Lys Ile Ser Glu Gln Gln Ala Glu Lys Ile Leu Lys Ser Met Asp Lys
     115 120 125
As Gly Thr Met Thr Ile Asp Trp Asn Glu Trp Arg Asp Tyr His Leu 130 $140$
Ser Thr Ile Phe Asp Val Gly Glu Asn Leu Thr Val Pro Asp Glu Phe
          165 170 175
Thr Val Glu Glu Arg Gln Thr Gly Met Trp Trp Arg His Leu Val Ala
180 185 190
Gly Gly Gly Ala Gly Ala Val. Ser Arg Thr Cys Thr Ala Pro Leu Asp
195 200 205
Arg Leu Lys Val Leu Met Gln Val His Ala Ser Arg Ser Asn Asn Met
 210 215 220
Cys Ile Val Gly Gly Phe Thr Gln Met Ile Arg Glu Gly Gly Ala Lys 225 230 235 240
                230
Ser Leu Trp Arg Gly Asn Gly Ile Asn Val Leu Lys Ile Ala Pro Glu
245 250 . 255
Ser Ala Ile Lys Phe Met Ala Tyr Glu Gln Met Lys Arg Leu Val Gly
    260 265 270
```

Ser Asp Gln Glu Thr Leu Arg Ile His Glu Arg Leu Val Ala Gly Ser 275 280 285

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Leu Ala Gly Ala Ile Ala Gln Ser Ser Ile Tyr Pro Met Glu Val Leu
 290 295 300
Lys Thr Arg Met Ala Leu Arg Lys
305
                 310
     <210> 143
    <211> 163
     <212> PRT
     <213> Rat
    <400> 143
Met Pro Leu Val Thr Thr Leu Phe Tyr Ala Cys Phe Tyr His Tyr Thr
              5
                              10
Glu Ser Glu Gly Thr Phe Ser Ser Pro Val Asn Leu Lys Lys Thr Phe 20 25 30
Lys Ile Pro Asp Arg Gln Tyr Val Leu Thr Ala Leu Ala Ala Arg Ala
    35 40
                                45
Lys Leu Arg Ala Trp Asn Asp Val Asp Ala Leu Phe Thr Thr Lys Asn
                  55
Trp Leu Gly Tyr Thr Lys Lys Arg Ala Pro Ile Gly Phe His Arg Val 65 70 70 75 80
Val Glu Ile Leu His Lys Asn Ser Ala Pro Val Gln Ile Leu Gln Glu
       85 90 95
Tyr Val Asn Leu Val Glu Asp Val Asp Thr Lys Leu Asn Leu Ala Thr
        100
                           105 110
Lys Phe Lys Cys His Asp Val Val Ile Asp Thr Cys Arg Asp Leu Lys 115 125
Asp Arg Gln Gln Leu Leu Ala Tyr Arg Ser Lys Val Asp Lys Gly Ser 130 135 140
Ala Glu Glu Lys Ile Asp Val Ile Leu Ser Ser Gln Ile Arg
145 150 155
Trp Lys Asn
    <210> 144
    <211> 330
    <212> PRT
    <213> Rat
    <400> 144
Met Ala Gly Trp Ala Gly Ala Glu Leu Ser Val Leu Asn Pro Leu Arg
1 5 10 15
Ala Leu Trp Leu Leu Ala Ala Ala Phe Leu Leu Ala Leu Leu Leu
          20
                           25
Gln Leu Ala Pro Ala Arg Leu Leu Pro Ser Cys Ala Leu Phe Gln Asp
    35
              40
                                        45
Leu Ile Arg Tyr Gly Lys Thr Lys Gln Ser Gly Ser Arg Arg Pro Ala 50 55
Val Cys Arg Ala Phe Asp Val Pro Lys Arg Tyr Phe Ser His Phe Tyr 65 70 75 80
Val Val Ser Val Leu Trp Asn Gly Ser Leu Leu Trp Phe Leu Ser Gln
            85 90 95
Ser Leu Phe Leu Gly Ala Pro Phe Pro Ser Trp Leu Trp Ala Leu Leu 100
Arg Thr Leu Gly Val Thr Gln Phe Gln Ala Leu Gly Met Glu Ser Lys 115 120 125
Ala Ser Arg Ile Gln Ala Gly Glu Leu Ala Leu Ser Thr Phe Leu Val
```

```
1.30
                       135
                                             1.40
Leu Val Phe Leu Trp Val His Ser Leu Arg Arg Leu Phe Glu Cys Phe 145 150 155
Tyr Val Ser Val Phe Ser Asn Thr Ala Ile His Val Val Gln Tyr Cys
             165 170 175
Phe Gly Leu Val Tyr Tyr Val Leu Val Gly Leu Thr Val Leu Ser Gln
180 185 190
Val Pro Met Asn Asp Lys Asn Val Tyr Ala Leu Gly Lys Asn Leu Leu
195 200 205
Leu Gln Ala Arg Trp Phe His Ile Leu Gly Met Met Met Phe Phe Trp
 210 215 220
Ser Ser Ala His Gln Tyr Lys Cys His Val Ile Leu Ser Asn Leu Arg
225 230
                              235
Arg Asn Lys Lys Gly Val Val Ile His Cys Gln His Arg Ile Pro Phe
245 250 255
Gly Asp Trp Phe Glu Tyr Val Ser Ser Ala Asn Tyr Leu Ala Glu Leu
260 265 270
Met Ile Tyr Ile Ser Met Ala Val Thr Phe Gly Leu His Asn Val Thr
275 280 285
Trp Trp Leu Val Val Thr Tyr Val Phe Phe Ser Gln Ala Leu Ser Ala 290 295 300
Phe Phe Asn His Arg Phe Tyr Lys Ser Thr Phe Val Ser Tyr Pro Lys 305 310 315 320
His Arg Lys Ala Phe Leu Pro Phe Leu Phe
              325
     <210> 145
     <211> 301
      <212> PRT
      <213> Rat
     <400> 145
Met Leu Val Ala Phe Leu Gly Ala Ser Ala Val Thr Ala Ser Thr Gly
                                 10
Leu Leu Trp Lys Lys Ala His Ala Glu Ser Pro Pro Ser Val Asn Ser 20 25 30
Lys Lys Thr Asp Ala Gly Asp Lys Gly Lys Ser Lys Asp Thr Arg Glu \cdot 35 40
Val Ser Ser His Glu Gly Ser Ala Ala Asp Thr Ala Ala Glu Pro Tyr
 50 55
Pro Glu Glu Lys Lys Lys Lys Arg Ser Gly Phe Arg Asp Arg Lys Val 65 70 75 80
Met Glu Tyr Glu Asn Arg Ile Arg Ala Tyr Ser Thr Pro Asp Lys Ile
85 90 95
Phe Arg Tyr Phe Ala Thr Leu Lys Val Ile Asn Glu Pro Gly Glu Thr
          100 105 110
Glu Val Phe Met Thr Pro Gln Asp Phe Val Arg Ser Ile Thr Pro Asn 115 120 . 125
Glu Lys Gln Pro Glu His Leu Gly Leu Asp Gln Tyr Ile Ile Lys Arg
130 135 140
Phe Asp Gly Lys Lys Ile Ala Gln Glu Arg Glu Lys Phe Ala Asp Glu 145 \, 150 \, 155 \, 160
Gly Ser Ile Phe Tyr Thr Leu Gly Glu Cys Gly Leu Ile Ser Phe Ser 165 170 175
Asp Tyr Ile Phe Leu Thr Thr Val Leu Ser Thr Pro Gln Arg Asn Phe 180 180 185
Glu Ile Ala Phe Lys Met Phe Asp Leu Asn Gly Asp Gly Glu Val Asp
```

```
195
                       200
                                        205
Met Glu Glu Phe Glu Gln Val Gln Ser Ile Ile Arg Ser Gln Thr Ser 210 215 220
Met Gly Met Arg His Arg Asp Arg Pro Thr Thr Gly Asn Thr Leu Lys
225 230 235
Ser Gly Leu Cys Ser Ala Leu Thr Thr Tyr Phe Phe Gly Ala Asp Leu 245 250 255
Lys Gly Lys Leu Thr Ile Lys Asn Phe Leu Glu Phe Gln Arg Lys Leu 260 265 270
Gln Arg Cys Leu Leu Gly Leu Pro Val Trp Glu Gly Ser Pro His Leu
   275 280 285
Pro Thr Gly His Trp Leu Arg Glu Leu Trp Ser Leu Leu
                 295 300
    <210> 146
    <211> 61
    <212> PRT
    <213> Rat
    <400> 146
Met Glu Asn Ile Tyr Tyr Thr Asn Leu Ile Thr Ile Leu Gly Asn Lys
                     10
1
His Ala Asn Gln Met Glu Leu Asn Leu Gln Ala Leu Ile Leu Ser Pro
 20 25
Trp Phe Ala Val Cys Ala Pro Pro Gly Phe Ala Arg Asp Gln Ala Val
    35
               40
Arg Gly Leu Ala Leu Ala Gly Arg Arg Ile Thr Val Val
                    55
    <210> 147
     <211> 105
     <212> PRT
     <213> Rat
     <400> 147
Met Leu Arg Arg Gln Leu Val Trp Trp His Leu Leu Ala Leu Leu Phe
 1 5
                              10 15
Leu Pro Phe Cys Leu Cys Gln Asp Glu Tyr Met Glu Ser Pro Gln Ala
                  25 . 30
     20
Gly Gly Leu Pro Pro Asp Cys Ser Lys Cys Cys His Gly Asp Tyr Gly 35 40 45
Phe Arg Gly Tyr Gln Gly Pro Pro Gly Pro Pro Gly Pro Pro Gly Ile
                  55
                            60
Pro Gly Asn His Gly Asn Asn Gly Asn Asn Gly Ala Thr Gly His Glu
       70 75
Gly Ala Lys Gly Glu Lys Gly Asp Lys Gly Asp Leu Gly Pro Arg Gly 85 90 95
Glu Arg Gly Gln His Gly Pro Lys Gly
     <210> 148
     <211> 210
     <212> PRT
     <213> Rat
     <400> 148
Met Leu Gly Ala Thr Ser Leu Ser Trp Pro Trp Val Leu Trp Ala Val
```

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5
                                10
Ala Gln Arg Asp Ser Val Asp Ala Ile Gly Met Phe Leu Gly Gly Leu 20 25 30
Val Ala Thr Ile Phe Leu Asp Ile Ile Tyr Ile Ser Ile Phe Tyr Ser
 35 40 45
Ser Val Ala Val Gly Asp Thr Gly Arg Phe Ser Ala Gly Met Ala Ile
                  55
                                 60
Phe Ser Leu Leu Leu Gln Ala Leu Leu Leu Leu Pro Arg Leu Pro His
Ala Pro Gly Ser Glu Gly Val Ser Ser Arg Ser Ala Arg Ile Ser Ser
85 90 95
Asp Leu Leu Arg Asn Ile Val Pro Thr Arg Gln Leu Thr Arg Gln Thr
                          105
          100
                                       110
His Leu Gln Thr Pro Leu Gln Ala Trp Arg Thr Arg Ala Lys Leu Pro
    115
               1.20
                                  125
Pro Gly Gly Thr Glu Ala Val Pro Gly Arg Pro Gly Ala Gln Gln Asp
130 135 140
Ala Cys His Leu Leu Tyr Trp Thr Tyr Asn Gly Val Ser Ser Ile Pro
145 150 155 160
Cys His Arg Gly Gly Leu Ser His Val Pro Ser Glu Val Pro Ala Glu
           165 170 175
Lys Ser Pro Val Leu Ile Leu His Ala Ala Pro Pro Phe Lys Thr Pro
180 185 190
Val Asn Pro Trp Ala Arg Thr Val Val Gly Phe Phe Pro Ser Ser Pro
           200
Ser Leu
  210
     <210> 149
     <211> 301
     <212> PRT
     <213> Rat
     <400> 149
Met Leu Val Ala Phe Leu Gly Ala Ser Ala Val Thr Ala Ser Thr Gly
            5
                               10
Leu Leu Trp Lys Lys Ala His Ala Glu Ser Pro Pro Ser Val Asn Ser
         20
                             25
Lys Lys Thr Asp Ala Gly Asp Lys Gly Lys Ser Lys Asp Thr Arg Glu
               40
Val Ser Ser His Glu Gly Ser Ala Ala Asp Thr Ala Ala Glu Pro Tyr
  50 55
                          60
Pro Glu Glu Lys Lys Lys Arg Ser Gly Phe Arg Asp Arg Lys Val 65 70 75 80
Met Glu Tyr Glu Asn Arg Ile Arg Ala Tyr Ser Thr Pro Asp Lys Ile
85 90 95 .
            85
                               90 95
Phe Arg Tyr Phe Ala Thr Leu Lys Val Ile Asn Glu Pro Gly Glu Thr 100 105 110
Glu Val Phe Met Thr Pro Gln Asp Phe Val Arg Ser Ile Thr Pro Asn 115 120 125
Glu Lys Gln Pro Glu His Leu Gly Leu Asp Gln Tyr Ile Ile Lys Arg
  130 135 140
Phe Asp Gly Lys Lys Ile Ala Gln Glu Arg Glu Lys Phe Ala Asp Glu 145 150 155 160
Gly Ser Ile Phe Tyr Thr Leu Gly Glu Cys Gly Leu Ile Ser Phe Ser
                             170
            165
                                               175
Asp Tyr Ile Phe Leu Thr Thr Val Leu Ser Thr Pro Gln Arg Asn Phe
```

```
180
                        185
Glu Ile Ala Phe Lys Met Phe Asp Leu Asn Gly Asp Gly Glu Val Asp 195 200 205
Met Glu Glu Phe Glu Gln Val Gln Ser Ile Ile Arg Ser Gln Thr Ser
 210 215 220
Lys Gly Lys Leu Thr Ile Lys Asn Phe Leu Glu Phe Gln Arg Lys Leu
  260 265 270
Gln Arg Cys Leu Leu Gly Leu Pro Val Trp Glu Gly Ser Pro His Leu
    275 280 285
Pro Thr Gly His Trp Leu Arg Glu Leu Trp Ser Leu Leu
                 295
    <210> 150
    <211> 80
    <212> PRT
    <213> Human
    <400> 150
Met Lys Leu Ser Gly Met Phe Leu Leu Ser Leu Ala Leu Phe Cys
1 5
Phe Leu Thr Gly Val Phe Ser Gln Gly Gly Gln Val Asp Cys Gly Glu 20 25 30
 20 25
Phe Gln Asp Thr Lys Val Tyr Cys Thr Arg Glu Ser Asn Pro His Cys 35 40 45
Gly Ser Asp Gly Gln Thr Tyr Gly Asn Lys Cys Ala Phe Cys Lys Ala
 50 55 60
Ile Val Lys Ser Gly Gly Lys Ile Ser Leu Lys His Pro Gly Lys Cys
               70
    <210> 151
    <211> 27
    <212> PRT
    <213> mouse
    <400> 151
Met Leu Lys Ala Ser Leu His Ile Leu Phe Leu Gly Ile Leu Asn Val
         5 10
Pro Ile Val Asp Thr Ser Thr Lys Thr Gly Val
                  25
     20
    <210> 152
    <211> 86
    <212> PRT
    <213> mouse
    <400> 152
Met Leu Gln Gly Pro Ala Pro Ser Cys Phe Trp Val Phe Ser Gly Ile 1 5 10 15
Cys Val Phe Trp Asp Phe Ile Phe Ile Ile Phe Phe Asn Val Leu Ser
      20 25 30
Leu Gly Asn Arg Glu Ile Ser Ala Lys Asp Phe Ala Asp Gln Pro Ala 35 40 45
Gly Ala Gln Gly Met Trp Gly Ile Trp Gly His Thr Ile Thr Cys Gly
```

```
55
                                          60
Leu Ala Pro Gly Ala Lys Pro Cys Ser Leu Lys Arg Glu Gly Pro Asp 65 70 75 80
Leu Leu Ser Phe Pro Pro
    85
     <210> 153
     <211> 72
     <212> PRT
     <213> mouse
    <400> 153
Met Ser Ala Ile Phe Asn Phe Gln Ser Leu Leu Thr Val Ile Leu Leu 1 5 10 10
Leu Ile Cys Thr Cys Ala Tyr Ile Arg Ser Leu Ala Pro Ser Ile Leu 20 25 30
Asp Arg Asn Lys Thr Gly Leu Leu Gly Ile Phe Trp Lys Cys Ala Arg
    35 40 45
Ile Gly Glu Arg Lys Ser Pro Tyr Val Ala Ile Cys Cys Ile Val Met 50 55 60
Ala Phe Ser Ile Leu Phe Ile Gln
     <210> 154
     <211> 169
     <212> PRT
     <213> mouse
    <400> 154
Met Ser Gly Leu Arg Thr Leu Leu Gly Leu Gly Leu Leu Val Ala Gly
1 5
                                  10
Ser Arg Leu Pro Arg Val Ile Ser Gln Gln Ser Val Cys Arg Ala Arg 20 25 30
Pro Ile Trp Gly Thr Gln Arg Arg Gly Ser Glu Thr Met Ala Gly 35 40
Ala Ala Val Lys Tyr Leu Ser Gln Glu Glu Ala Gln Ala Val Asp Gln
50 60
Glu Leu Phe Asn Glu Tyr Gln Phe Ser Val Asp Gln Leu Met Glu Leu
65 70 75 80
Ala Gly Leu Ser Cys Ala Thr Ala Ile Ala Lys Ala Tyr Pro Pro Thr
85 90
Ser Met Ser Lys Ser Pro Pro Thr Val Leu Val Ile Cys Gly Pro Gly
100 105 110
Asn Asn Gly Gly Asp Gly Leu Val Cys Ala Arg His Leu Lys Leu Phe
115 120 125
Gly Tyr Gln Pro Thr Ile Tyr Tyr Pro Lys Arg Pro Asn Lys Pro Leu
130 135 140 ...
Phe Thr Gly Leu Val Thr Gln Cys Gln Lys Met Asp Ile Pro Phe Leu
145 150 155 160
Gly Glu Met Pro Pro Glu Asp Gly Met
              165
     <210> 155
     <211> 61
     <212> PRT
     <213> mouse
```

<400> 155

```
Met Glu Lys Gln Met Asp Ala Ser Val Ser Val Ile Phe Gly Ser Ile
           5
                     10
Val Ile Ser Ala Phe Leu Tyr Leu Ser Leu Ala Gly Pro Trp Ala Val
                       25
Thr Val Thr Gln Met Arg Thr Ile Ile Ile Thr Met Asp Gln Leu Arg
  35 40
Asp Ala Leu Ile Leu Asp Glh Leu Lys Val Ala Val Ser
                    55
   50
    <210> 156
    <211> 131
    <212> PRT
    <213> mouse
   <400> 156
Met Ala Pro Ser Leu Trp Lys Gly Leu Val Gly Val Gly Leu Phe Ala
              5
                              10
Leu Ala His Ala Ala Phe Ser Ala Ala Gln His Arg Ser Tyr Met Arg
20 25 30
Leu Thr Glu Lys Glu Asp Glu Ser Leu Pro Ile Asp Ile Val Leu Gln
 35 40 45
Thr Leu Leu Ala Phe Ala Val Thr Cys Tyr Gly Ile Val His Ile Ala
                   55
Gly Glu Phe Lys Asp Met Asp Ala Thr Ser Glu Leu Lys Asn Lys Thr 65 70 75 80
    70
Phe Asp Thr Leu Arg Asn His Pro Ser Phe Tyr Val Phe Asn His Arg
          85 90 9<del>5</del>
Gly Arg Val Leu Phe Arg Pro Ser Asp Ala Thr Asn Ser Ser Asn Leu
       100 105 110
Asp Ala Leu Ser Ser Asn Thr Ser Leu Lys Leu Arg Lys Phe Asp Ser
Leu Arg Arg
   130
    <210> 157
    <211> 133
     <212> PRT
    <213> mouse
    <400> 157
Met Arg Leu Leu Ala Ala Ala Leu Leu Leu Leu Leu Ala Leu Cys
                            10
Ala Ser Arg Val Asp Gly Ser Lys Cys Lys Cys Ser Arg Lys Gly Pro 20 25 30
Lys Ile Arg Tyr Ser Asp Val Lys Lys Leu Glu Met Lys Pro Lys Tyr 35 40 45.
Pro His Cys Glu Glu Lys Met Val Ile Val Thr Thr Lys Glu His Val
  50
                55
                                   60
Gln Gly Thr Gly Ala Arg Ser Thr Ala Cys Thr Leu Ser Cys Arg Ala
              70
                               75
Pro Asn Ala Ser Ser Ser Gly Thr Met Pro Gly Thr Arg Ser Ala Gly
                            90 95
         85
Ser Thr Lys Asn Arg Val Asp Asp His Gly Lys Lys Asn Ser Arg Pro
        100
                          105
                                          110
Val Glu Arg Leu Gln Gln Arg Thr Leu Gln Ile Lys Ile Lys Ala Leu
                       120 ,
```

```
Ser Phe Ser Gln Ala
   130
     <210> 158
     <211> 78
     <212> PRT
     <213> mouse
     <400> 158
Gly Thr Arg Lys Pro Leu Pro Met Glu Ala His Ser Arg Arg Glu Lys
            5
                                10
                                                   1.5
Ala Ser Gly Leu Arg Leu Ala Trp His Tyr Glu Cys Ser Gly Val Ser
   20 25 30
Val Trp Trp Met Cys Val Leu Gly Trp Leu Ser Phe Leu Val Phe Leu
35 40 45
Leu Phe Ser Leu Val Cys Ser Phe Pro Ser Pro Ile Asn His Ser His
                    55 60
Met Leu Pro Cys Leu Phe Leu Arg Gly Gly Gly Ser Asn Val
                  70
     <210> 159
     <211> 206
     <212> PRT
     <213> mouse
     <400> 159
Met Leu Pro Pro Ala Ile His Leu Ser Leu Ile Pro Leu Leu Cys Ile
1 5 10 15
Leu Met Arg Asn Cys Leu Ala Phe Lys Asn Asp Ala Thr Glu Ile Leu
                                      30
 20 . 25
Tyr Ser His Val Val Lys Pro Val Pro Ala His Pro Ser Ser Asn Ser
   35 40 45
Thr Leu Asn Gln Ala Arg Asn Gly Gly Arg His Phe Ser Ser Thr Gly 50 55 60
Lieu Asp Arg Asn Ser Arg Val Gln Val Gly Cys Arg Glu Leu Arg Ser 65 70 75 80
Thr Lys Tyr Ile Ser Asp Gly Gln Cys Thr Ser Ile Ser Pro Leu Lys
85 90
Glu Leu Val Cys Ala Gly Glu Cys Leu Pro Leu Pro Val Leu Pro Asn
100 105 110
Trp Ile Gly Gly Tyr Gly Thr Lys Tyr Trp Ser Arg Arg Ser Ser
115 120 125
Gln Glu Trp Arg Cys Val Asn Asp Lys Thr Arg Thr Gln Arg Ile Gln 130 135 140
Leu Gln Cys Gln Asp Gly Ser Thr Arg Thr Tyr Lys Ile Thr Val Val 145 150 150 155
Thr Ala Cys Lys Cys Lys Arg Tyr Thr Arg Gln His Asn Glu Ser Sér 165 170 175
His Asn Phe Glu Ser Val Ser Pro Ala Lys Pro Ala Gln His His Arg
        180 185 190
Glu Arg Lys Arg Ala Ser Lys Ser Ser Lys His Ser Leu Ser
                200 205
      195
      <210> 160
      <211> 169
      <212> PRT
      <213> mouse
```

```
<400> 160
Met Ser Gly Leu Arg Thr Leu Leu Gly Leu Gly Leu Leu Val Ala Gly 1 5 10 10 10
Ser Arg Leu Pro Arg Val Ile Ser Gln Gln Ser Val Cys Arg Ala Arg
         20
                           25
Pro Ile Trp Trp Gly Thr Gln Arg Arg Gly Ser Glu Thr Met Ala Gly
     35 ` 40
Ala Ala Val Lys Tyr Leu Ser Gln Glu Glu Ala Gln Ala Val Asp Gln 50 \phantom{\bigg|}55\phantom{\bigg|}
Glu Leu Phe Asn Glu Tyr Gln. Phe Ser Val Asp Gln Leu Met Glu Leu 65 70 75 80
Ala Gly Leu Ser Cys Ala Thr Ala Ile Ala Lys Ala Tyr Pro Pro Thr 85 90 95
Ser Met Ser Lys Ser Pro Pro Thr Val Leu Val Ile Cys Gly Pro Gly 100 105 110
Asn Asn Gly Gly Asp Gly Leu Val Cys Ala Arg His Leu Lys Leu Phe
115 120 125
Gly Tyr Gln Pro Thr Ile Tyr Tyr Pro Lys Arg Pro Asn Lys Pro Leu
 130 135 140
Phe Thr Gly Leu Val Thr Gln Cys Gln Lys Met Asp Ile Pro Phe Leu
145 150 155 160
Gly Glu Met Pro Pro Glu Asp Gly Met
     <210> 161
     <211> 114
      <212> PRT
      <213> mouse
     <400> 161
Met Ser Val Thr Ile Gly Arg Leu Ala Leu Phe Leu Ile Gly Ile Leu 1 5 5 10 10 10
Leu Cys Pro Val Ala Pro Ser Leu Thr Arg Ser Trp Pro Gly Pro Asp 20 25 30
                             25
Thr Cys Ser Leu Phe Leu Gln His Ser Leu Ser Leu Ser Leu Arg Leu
      35
                   40
                                              45
Gly Gln Ser Leu Glu Gly Gly Leu Ser Val Cys Phe His Val Cys Ile
50 55 60
His Ala Cys Glu Cys Val Ala Cys Cys Arg Val Leu Trp Asp Pro Lys 65 70 75 80
Pro Arg Gly Ser Ser Leu Cys Arg Trp Val Leu Gly Ser Ile Thr Cys
           85
                         90
Leu Phe Met Tyr Glu Val Gly Gly Trp Thr Gln Gly Gly Leu Ile Val
100 105 110
                     105
Ser Leu
```

<210> 162

<211> 46

<212> PRT

<213> mouse

<400> 162

Met His Tyr Pro Cys Leu Ala Cys Leu Phe Val Asn Val His Trp Cys 1 5 5 10 10 15 15 Phe Ala Trp Met Cys Ile Leu Val Lys Met Ser Glu Leu Leu Glu Leu

```
25
Glu Leu Glu Thr Met Val Ser Cys Leu Val Asp Val Gly Asn
    35 40
     <210> 163
     <211> 122
     <212> PRT
     <213> mouse
    <400> 163
Met Phe Thr Phe Val Val Leu Val Ile Thr Ile Val Ile Cys Leu Cys
1
          5 . 10
His Val Cys Phe Gly His Phe Lys Tyr Leu Ser Ala His Asn Tyr Lys
 20 25
Ile Glu His Thr Glu Thr Asp Ala Val Ser Ser Arg Ser Asn Gly Arg
35 40 45
Pro Pro Thr Ala Gly Ala Val Pro Lys Ser Ala Lys Tyr Ile Ala Gin 50 60
Val Leu Gln Asp Ser Glu Gly Asp Gly Asp Gly Asp Gly Ala Pro Gly 65 70 75 80
Ser Ser Gly Asp Glu Pro Pro Ser Ser Ser Gln Asp Glu Glu Leu
85 90
Leu Met Pro Pro Asp Gly Leu Thr Asp Thr Asp Phe Gln Ser Cys Glu
  100 . 105
Asp Ser Leu Ile Glu Asn Glu Ile His Gln
    115 120
    <210> 164
    <211> 60
     <212> PRT
    <213> Rat
    <400> 164
Met Ser Phe Val Lys Ile Glu Ala Thr Pro Thr Gln Thr Lys Trp Pro 1 . 5
Phe Ser Val Val Pro Gln Ser Leu Leu Val Thr Val Tyr Ile Cys Tyr
  20 25
                                         30
Ile Phe Leu Val Ile Phe Phe Phe Phe Glu Ala Cys Gln Glu Val
 35 40 45
Leu Cys Ser Phe Phe Asp Phe Ser Arg Arg Gly
             55
    <210> 165
    <211> 57
    <212> PRT
    <213> mouse
    <400> 165
Met Gly Ser Pro Ile Ser Gly Val Cys Pro Val Leu Pro Gly Gly Leu 1 5 10 10
Phe Val Ala Leu Gly Trp Ile Phe Leu Leu Phe His Arg Asp Ala Phe
 20 25 30
Ser Leu His Thr Met Ser Ala Gly Phe Pro Lys Ser Pro Ala Asn Pro
 35 40
                              45
His His Pro Pro Leu Arg Leu Ser Pro
                   55
```

```
<210> 166
    <211> 75
    <212> PRT
    <213> mouse
    <400> 166
Lys Thr Arg Arg Thr Leu Thr Gly Gln Leu Gly Leu Phe Ser Val Asp
          5 ` 10 15
Phe Met Val Cys Ile Phe Leu Phe Leu Phe Phe Cys Phe Leu Phe Pro
20 25 30
Phe Pro Leu Phe Leu Val Arg Lys His Ile Leu Leu Ser His Cys Lys 35 40 45
                                 45
Gln Trp Glu Gly Ser Thr Met Thr His Thr His Thr His Ile
 50 55 60
His Ile His Thr Pro Pro Arg Gln Cys Gln Ser
  70
65
   <210> 167
    <211> 52
    <212> PRT
    <213> mouse
   <400> 167
Val Arg Ser Leu Glu Gln Leu Gly Leu Phe Ser Val Asp Phe Met Val
1. 5
                         10
Cys Ile Phe Leu Phe Leu Phe Phe Cys Phe Leu Phe Pro Phe Pro Leu
  20 25 30
Phe Leu Val Arg Lys His Ile Leu Leu Ser His Cys Lys Gln Trp Glu
35 40
Gly Ser Thr Met
 50
   <21Ò> 168
   <211> 119
    <212> PRT
    <213> Rat
   <400> 168
Met Leu Gly Ala Thr Ser Leu Ser Trp Pro Trp Val Leu Trp Ala Val
         5 10 15
Ala Gln Arg Asp Ser Val Asp Ala Ile Gly Met Phe Leu Gly Gly Leu
 20 25 30
Val Ala Thr Ile Phe Leu Asp Ile Ile Tyr Ile Ser Ile Phe Tyr Ser
   35
                    40
                                 45
Ser Val Ala Val Gly Asp Thr Gly Arg Phe Ser Ala Gly Met Ala Ile
50 55 . 60
Phe Ser Leu Leu Gln Ala Leu Leu Leu Leu Pro Arg Leu Pro His 65 70 75 80
Ala Pro Gly Ser Glu Gly Val Ser Ser Arg Ser Ala Arg Ile Ser Ser 85 90 95
Asp Leu Leu Arg Asn Ile Val Pro Thr Arg Gln Leu Thr Arg Gln Thr
   100 105 110
His Leu Gln Thr Pro Leu Gln
      115
    <210> 169
    <211> 104
```

<212> PRT

```
<213> Rat
      <220>
     <400> 169
Leu Val Pro Lys Ser Ala Arg Ala Ser Leu Leu Cys Cys Gly Pro Lys 1 5 10 10
Leu Ala Ala Cys Gly Ile Val Leu Ser Ala Trp Gly Val Ile Met Leu 20 25 330
        20
                          25
Ile Met Leu Gly Ile Phe Phe Asn Val His Ser Ala Val Xaa Ile Xaa
  35 40 45
Asp Val Pro Phe Thr Glu Lys Asp Phe Glu Asn Gly Pro Gln Asn Ile 50 55 60
Tyr Asn Leu Tyr Glu Gln Val Ser Tyr Asn Cys Phe Ile Ala Ala Gly
65 70 75 80
Leu Tyr Leu Leu Xaa Gly Gly Phe Ser Phe Cys Gln Val Arg Leu Asn
85 90 95
Lys Arg Lys Glu Tyr Met Val Arg
    100
     <210> 170
     <211> 123
                         .
     <212> PRT
     <213> Rat
     <220>
     <221> UNSURE
     <222> (27)...(27)
     <221> UNSURE
     <222> (104)...(104)
     <221> UNSURE
     <222> (118)...(118)
    <400> 170
Met Arg Pro Gly Ala Asp Trp Ala Ala Val Cys Ala Leu Trp Pro Ser 1 \hspace{1.5cm} 5 \hspace{1.5cm} 10 \hspace{1.5cm} 15
Trp Arg Pro Ser Cys Ser Leu Pro Ser Ser Xaa Arg Ile Gln Pro Asp
       20 25
Glu Leu Trp Leu Tyr Arg Asn Pro Tyr Val Lys Ala Glu Tyr Phe Pro
  35 40
                                         45
Thr Gly Pro Met Phe Val Ile Ala Phe Leu Thr Pro Leu Ser Leu Ile 50 60
Phe Phe Ala Lys Phe Leu Arg Lys Ala Asp Ala Asp Arg Gln Arg Ala
65 . 70 75 80
Ser Leu Pro Arg Cys Gln Pro Cys Pro Ser Ala Lys Trp Cys Leu Tyr
85 90 95
Gln His His Lys Thr Asp Ser Xaa Gln Gly His Ala Gln Ile Ala Ser
100 105 110
Thr Glu Cys Ser Pro Xaa Gly Ile Ala His Ser
                         120
     <210> 171
     <211> 75
```

<212> PRT

```
<213> Rat
     <400> 171
Ser Ala Gly Val Met Thr Ala Ala Val Phe Phe Gly Cys Ala Phe Ile
                            10
Ala Phe Gly Pro Ala Leu Ser Leu Tyr Val Phe Thr Ile Ala Thr Asp
20 25 30
Pro Leu Arg Val Ile Phe Leu Ile Ala Gly Ala Phe Phe Trp Leu Val
  35 40
                              45
Ser Leu Leu Leu Ser Ser Val Phe Trp Phe Leu Val Arg Val Ile Thr
 50 55
Asp Asn Arg Asp Gly Pro Val Gln Asn Tyr Leu
65 . 70
    <210> 172
     <211> 79
     <212> PRT
     <213> Human
     <400> 172
Lys Thr Ser Tyr His Tyr His Thr Asn Val Glu Glu Leu Thr Ile Pro
1 5 10 15
Glu Thr Arg Asn Asn Leu Tyr Ile Ser Ile Ser Trp Leu Trp Cys Leu
        20
                        25
                                      30
Val Leu Val Leu Leu Ser Thr Met Ile Leu Asn Lys His Gly Trp Met
    35
            40
Lys Ala Asn Ala Tyr Ser Leu Val Pro Ser Ile Ile Tyr Ser Pro Ser
 50 55 60
Tyr Leu Lys Leu Leu Leu Arg Leu Tyr Lys Leu Gln Ile Cys Cys
65 70 75
   <210> 173
<211> 134
    <212> PRT
    <213> Human
    <220>
<400> 173
Leu Arg Gly Arg Gly Val Cys Ser Gln Glu Ser Phe Gly Gly
            5
Cys Cys Val Ser Gly Leu Ile Ala Met Gly Thr Lys Ala Gln Val Glu
  20
                       25
Arg Lys Leu Ceu Cys Leu Phe Ile Leu Ala Ile Leu Leu Cys Ser Leu
 35
             40 45
Ala Leu Gly Ser Val Thr Val His Ser Ser Glu Pro Glu Val Arg Ile
  50 55
                      60 ....
Pro Glu Asn Asn Pro Val Lys Leu Ser Cys Ala Tyr Ser Gly Phe Ser
65 70
                             75
Ser Pro Arg Val Glu Trp Lys Phe Asp Gln Gly Asp Thr Thr Arg Leu
                   90
          85
Val Cys Tyr Asn Asn Lys Ile Thr Ala Ser Tyr Glu Asp Arg Val Thr
                      105 . 110
        100
Phe Leu Pro Thr Gly Ile Thr Phe Lys Ser Val Thr Arg Glu Asp Thr
   115 120 125
Gly Thr Tyr Thr Cys Met
  130
```

```
<210> 174
     <211> 137
     <212> PRT
     <213> Human
     <400> 174
Ala Trp Ser Arg Pro Arg Tyr Asp Ser Val Leu Ala Leu Ser Ala Ala 1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15
Leu Gln Ala Thr Arg Ala Leu Met Val Val Ser Leu Val Leu Gly Phe
                       25
    20
Leu Ala Met Phe Val Ala Thr Met Gly Met Lys Cys Thr Arg Cys Gly
 35
                      40
Gly Asp Asp Lys Val Lys Lys Ala Arg Ile Ala Met Gly Gly Gly Ile
50 55 60
Ile Phe Ile Val Ala Gly Leu Ala Ala Leu Val Ala Cys Ser Trp Tyr
65 70 75
Gly His Gln Ile Val Thr Asp Phe Tyr Asn Pro Leu Ile Pro Thr Asn
              85
                              90
Ile Lys Tyr Glu Phe Gly Pro Ala Ile Phe Ile Gly Trp Ala Gly Ser
100 105 110
Ala Leu Val Ile Leu Gly Gly Ala Leu Ser Pro Val Pro Val Leu Gly
115 120 125
Ile Arg Ala Gly Leu Gly Thr Cys Pro
                      135
     <210> 175
    <211> 43
    <212> PRT
    <213> Human
    <400> 175
Met Lys Leu Ser Gly Met Phe Leu Leu Leu Ser Leu Ala Leu Phe Cys 1 \hspace{1.5cm} 5 \hspace{1.5cm} 10 \hspace{1.5cm} 15
Phe Leu Thr Gly Val Phe Ser Gln Gly Gly Gln Val Asp Cys Gly Glu
 20 25
Ser Arg Thr Pro Arg Pro Thr Ala Leu Gly Asn
. 35 40
    <210> 176
    <211> 63
     <212> PRT
     <213> Rat
    <400> 176
Pro Asn Thr Arg Pro Arg Arg His Thr Ala Cys Arg Val Ser Ile Ser 1 5 10 ... 15
Val Phe Tyr Met Leu His Thr Glu Leu Lys Lys Cys Trp Phe Phe Leu
 20 25 30
Phe Cys Phe Ser Leu Phe Leu Trp Phe Cys Phe Trp Phe Cys Phe Leu
35 40 45
Leu Pro Arg Phe Asp Tyr Leu Pro Met Pro Ser Thr Arg Pro Arg
  50
                    55
                              60
    <210> 177
    <211> 52
    <212> PRT
```

```
<213> mouse
    <400> 177
Met Leu Gln Gly Pro Ala Pro Ser Cys Phe Trp Val Phe Ser Gly Ile
                             10
Cys Val Phe Trp Asp Phe Ile Phe Ile Ile Phe Phe Asn Val Leu Ser
                         25
Leu Gly Asn Arg Glu Ile Ser Ala Lys Asp Phe Ala Asp Gln Pro Ala
 35 40 ly Ala Gln Gly
                                 45
Gly Ala Gln Gly
  50 .
     <210> 178
     <211> 62
    <212> PRT
    <213> mouse
    <400> 178
Val Ser Pro Arg Pro Thr Tyr Pro Ser Thr Ala Ser Ser Met Ala Ala 1 5 5 10 10 15
Phe Leu Val Thr Gly Phe Phe Phe Ser Leu Phe Val Val Leu Gly Met
 20 25 30
Glu Pro Arg Ala Leu Phe Arg Pro Asp Lys Ala Leu Pro Leu Ser Cys
                     40
                                       45
Ala Lys Pro Thr Ser Leu Cys Val Gln Ser Ser Phe Leu Gly
  50 55
    <210> 179
     <211> 123
     <212> PRT
     <213> mouse
    <400> 179
Ala Ser Arg Thr Ala Val Met Ser Leu Cys Arg Cys Gln Gln Gly Ser
1 5 10 15
Arg Ser Arg Met Asp Leu Asp Val Val Asn Met Phe Val Ile Ala Gly
      20
                        25
                                             30
Gly Thr Leu Ala Ile Pro Ile Leu Ala Phe Val Ala Ser Phe Leu Leu 35 40 45
Trp Pro Ser Ala Leu Ile Arg Ile Tyr Tyr Trp Tyr Trp Arg Arg Thr 50 60
Leu Gly Met Gln Val Arg Tyr Ala His His Glu Asp Tyr Gln Phe Cys
                70
                               75
Tyr Ser Phe Arg Gly Arg Pro Gly His Lys Pro Ser Ile Leu Met Leu
85 90 95
His Gly Phe Ser Ala His Lys Gly His Val Ala Gln Arg Gly Gln Val
      100 105 . 110
Pro Ser Arg Lys Asn Leu His Phe Gly Cys Val
      115
                120
     <210> 180
     <211> 120
     <212> PRT
     <213> mouse
    <220>
    <221> UNSURE
```

```
<222> (5)...(5)
<400> 180
Ala Arg Arg Arg Kaa Arg Trp Arg Arg Gly Cys Cys Trp Leu Ile Gly
1 5 10
Thr Gly Leu Arg Ala Ala Thr Trp Thr Val Leu Cys Ser Pro Asn Ser
Ser Leu Val Val Ala Arg His Thr Lys Ser Phe Pro Pro Lys Lys Pro 35 40 45
Leu Gln Ala Leu Thr Met Ser Ile Met Asp His Ser Pro Thr Thr Gly 50 55 60
Val Val Thr Val Ile Val Ile Leu Ile Ala Ile Ala Ala Leu Gly Gly 65 70 75 80
Leu Ile Leu Gly Cys Trp Cys Tyr Leu Arg Leu Gln Arg Ile Ser Gln 85 90 95
Ser Glu Asp Glu Glu Ser Ile Val Gly Asp Gly Glu Thr Lys Glu Pro
       100 105 110
Phe Tyr Trp Cys Ser Thr Leu Leu
      115 120
     <210> 181
     <211> 60
     <212> PRT
     <213> mouse
     <400> 181
Lys Gly Pro Glu Val Ser Cys Cys Ile Lys Tyr Phe Ile Phe Gly Phe 1 5 5 10 10 15
Asn Val Ile Phe Trp Phe Leu Gly Ile Thr Phe Leu Gly Ile Gly Leu
    20 25 30
Trp Ala Trp Asn Glu Lys Gly Val Leu Ser Asn Ile Ser Ser Ile Thr 35 40 45
Asp Leu Gly Gly Phe Asp Pro Val Trp Leu Phe Leu
  50 . 55
    <210> 182
    <211> 72
    <212> PRT
    <213> mouse
    <220>
    <400> 182
Lys Pro Thr Val Gly Ser Ala Glu Val Ala Ile Ala Val Phe Leu Val .

1 5 10 15
Ile Cys Ile Ile Val Val Leu Thr Ile Leu Gly Tyr Cys Phe Phe Lys 20 25 30
Asn Gln Arg Lys Glu Phe His Ser Pro Leu His His Pro Pro Pro Thr 35 40 45
Pro Ala Ser Ser Thr Val Ser Thr Thr Glu Asp Thr Glu His Leu Val
 50 55 60 ...
Tyr Asn His Thr Thr Gln Pro Leu
              70
     <210> 183
     <211> 771
```

<212> PRT <213> Rat

<220>

<400> 183 Glu Leu Tyr Leu Asp Gly Asn Gln Phe Thr Leu Val Pro Lys Glu Leu 10 15 5 Ser Asn Tyr Lys His Leu Thr Leu Ile Asp Leu Ser Asn Asn Arg Ile 20 25 Ser Thr Leu Ser Asn Gln Ser Phe Ser Asn Met Thr Gln Leu Leu Thr 45 40 Leu Ile Leu Ser Tyr Asn Arg Leu Arg Cys Ile Pro Pro Arg Thr Phe 50 55 60 Asp Gly Leu Lys Ser Leu Arg Leu Leu Ser Leu His Gly Asn Asp Ile 70 75 Ser Val Val Pro Glu Gly Ala Phe Gly Asp Leu Ser Ala Leu Ser His 85 90 95 Leu Ala Ile Gly Ala Asn Pro Leu Tyr Cys Asp Cys Asn Met Gln Trp Leu Ser Asp Trp Val Lys Ser Glu Tyr Lys Glu Pro Gly Ile Ala Arg 115 120 125 Cys Ala Gly Pro Gly Glu Met Ala Asp Lys Leu Leu Leu Thr Thr Pro 140 130 135 Ser Lys Asn Phe Thr Cys Gln Gly Pro Val Asp Val Thr Ile Gln Ala 145 150 155 160Lys Cys Asn Pro Cys Leu Ser Asn Pro Cys Lys Asn Asp Gly Thr Cys 165 170 175 Asn Asn Asp Pro Val Asp Phe Tyr Arg Cys Thr Cys Pro Tyr Gly Phe 180 185 190 Lys Gly Gln Asp Cys Asp Val Pro Ile His Ala Cys Thr Ser Asn Pro 195 200 205 Cys Lys His Gly Gly Thr Cys His Leu Lys Pro Arg Arg Glu Thr Trp 210 215 220 Ile Trp Cys Thr Cys Ala Asp Gly Phe Glu Gly Glu Ser Cys Asp Ile 225 230 235 Asn Ile Asp Asp Cys Glu Asp Asn Asp Cys Glu Asn Asn Ser Thr Cys 245 250 250 Val Asp Gly Ile Asn Asn Tyr Thr Cys Leu Cys Pro Pro Glu Tyr Thr 260 265 270 Gly Glu Leu Cys Glu Glu Lys Leu Asp Phe Cys Ala Gln Asp Leu Asn 275 280 285 Pro Cys Gln His Asp Ser Lys Cys Ile Leu Thr Pro Lys Gly Phe Lys 290 295 300 290 295 300 Cys Asp Cys Thr Pro Gly Tyr Ile Gly Glu His Cys Asp Ile Asp Phe 305 310 315 320 Asp Asp Cys Gln Asp Asn Lys Cys Lys Asn Gly Ala His Cys Thr Asp 325 330 335 Ala Val Asn Gly Tyr Thr Cys Val Cys Pro Glu Gly Tyr Ser Gly Leu 340 345 350 Phe Cys Glu Phe Ser Pro Pro Met Val Phe Leu Arg Thr Ser Pro Cys 355 360 365 Asp Asn Phe Asp Cys Gln Asn Gly Ala Gln Cys Ile Ile Arg Val Asn 375 380 Glu Pro Ile Cys Gln Cys Leu Pro Gly Tyr Leu Gly Glu Lys Cys Glu 390 , 395

```
Lys Leu Val Ser Val Ser Ile Leu Val Asn Lys Glu Ser Tyr Leu Gln
            405 410 415
Ile Pro Ser Ala Lys Val Arg Pro Gln Thr Asn Ile Thr Leu Gln Ile
        420 425
Ala Thr Asp Glu Asp Ser Gly Ile Leu Leu Tyr Lys Gly Asp Lys Asp
     435
                        440
                                   445
His Ile Ala Val Glu Ser Ile Glu Gly Ile Arg Ala Ser Tyr Asp Thr
            455 460
Gly Ser His Pro Ala Ser Ala Ile Tyr Ser Val Glu Thr Ile Asn Asp
465 470 475 480
Gly Asn Phe His Ile Val Glu Leu Leu Thr Leu Asp Ser Ser Leu Ser
485 490 495
Leu Ser Val Asp Gly Gly Ser Pro Lys Ile Ile Thr Asn Leu Ser Lys 500 505
Gln Ser Thr Leu Asn Phe Asp Ser Pro Leu Tyr Val Gly Gly Met Pro 515 520 525
Gly Lys Asn Asn Val Ala Ser Leu Arg Gln Ala Pro Gly Gln Asn Gly 530 540
Thr Ser Phe His Gly Cys Ile Arg Asn Leu Tyr Ile Asn Ser Glu Leu 545 550 560
Gln Asp Phe Arg Lys Val Pro Met Gln Thr Gly Ile Leu Pro Gly Cys 565 570 576
Glu Pro Cys His Lys Lys Val Cys Ala His Gly Thr Cys Gln Pro Ser 580 585 590
Ser Gln Ser Gly Phe Thr Cys Glu Cys Glu Glu Gly Trp Met Gly Pro 595 600 605
                                             605
Leu Cys Asp Gln Arg Thr Asn Asp Pro Cys Leu Gly Asn Lys Cys Val 610 615 620
His Gly Thr Cys Leu Pro Ile Asn Ala Phe Ser Tyr Ser Cys Lys Cys
625 630 635 640
Leu Glu Gly His Gly Gly Val Leu Cys Asp Glu Glu Glu Asp Leu Phe
645 650 655
Asn Pro Leu Pro Gly Asp Gln Val Gln Ala Arg Glu Val Gln Ala Leu
660 665 670
Trp Ala Arg Ala Ala Leu Leu Trp Met Gln Gln Trp Ile His Arg Gly
    675 680 685
Gln Leu Thr Gln Arg Ile Ser Cys Arg Gly Glu Arg Ile Arg Asp Tyr
 690 695
Tyr Gln Ser Ser Arg Val Arg Cys Leu Ser Asn Asp
    <210> 184
```

<210> 184 <211> 340 <212> PRT <213> mouse

```
85
                                 90
Ser Leu Ile Ile Ala Leu Gly Asn Glu Asp Ala Leu Gly Glu Tyr Ser
100 105 110
Cys Thr Pro Tyr Asn Ser Leu Gly Thr Ala Gly Pro Ser Pro Val Thr
    115 120 125
Arg Val Leu Leu Lys Ala Pro Pro Ala Phe Ile Asp Gln Pro Lys Glu
130 135 140
Glu Tyr Phe Gln Glu Val Gly Arg Glu Leu Leu Ile Pro Cys Ser Ala
145 150 155 160
Arg Gly Asp Pro Pro Pro Ile Val Ser Trp Ala Lys Val Gly Arg Gly
            165 170 175
Leu Gln Gly Gln Ala Gln Val Asp Ser Asn Asn Ser Leu Val Leu Arg
          180 185 190
Pro Leu Thr Lys Glu Ala Gln Gly Arg Trp Glu Cys Ser Ala Ser Asn 195 200 205
Ala Val Ala Arg Val Thr Thr Ser Thr Asn Val Tyr Val Leu Gly Thr
 210 215 220
Ser Pro His Val Val Thr Asn Val Ser Val Val Pro Leu Pro Lys Gly 225 230 235 240
Ala Asn Val Ser Trp Glu Pro Gly Phe Asp Gly Gly Tyr Leu Gln Arg
245 250 255
Phe Ser Val Trp Tyr Thr Pro Leu Ala Lys Arg Pro Asp Arg Ala His 260 265 270
His Asp Trp Val Ser Leu Ala Val Pro Ile Gly Ala Thr His Leu Leu 275 280 285
Val Pro Gly Leu Gln Ala His Ala Gln Tyr Gln Phe Ser Val Leu Ala
 290 295 300
Gln Asn Lys Leu Gly Ser Gly Pro Phe Ser Glu Ile Val Leu Ser Ile 305 310 315 320
Pro Glu Gly Leu Pro Thr Thr Pro Ala Ala Pro Gly Leu Pro Ala Thr
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    325
Arg Ser Arg Val
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    <211> 536
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Thr Phe Asp Ala Gly Glu Phe Ala Gly Trp Glu Lys Val Gly Ser Gly
          20
                             25
                                                30
Gly Phe Gly Gln Val Tyr Lys Val Arg His Val His Trp Lys Thr Trp 35 45
                                          45
    35 . 40
Leu Ala Ile Lys Cys Ser Pro Ser Leu His Val Asp Asp Arg Glu Arg 50 60
Met Glu Leu Leu Glu Glu Ala Lys Lys Met Glu Met Ala Lys Phe Arg
                 70
                                  75
Tyr Ile Leu Pro Val Tyr Gly Ile Cys Gln Glu Pro Val Gly Leu Val
            85 90 95
Met Glu Tyr Met Glu Thr Gly Ser Leu Glu Lys Leu Leu Ala Ser Glu 100 105 110
Pro Leu Pro Trp Asp Leu Arg Phe Arg Ile Val His Glu Thr Ala Val
115 120 125
Gly Met Asn Phe Leu His Cys Met Ser Pro Pro Leu Leu His Leu Asp
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130
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Leu Lys Pro Ala Asn Ile Leu Leu Asp Ala His Tyr Gln Met Ser Arg
145 150 155
Phe Leu Asp Phe Gly Leu Ala Lys Cys Asn Gly Met Ser His Ser His
         165 170
                                175
Asp Leu Ser Met Asp Gly Leu Phe Gly Thr Ile Gly Tyr Leu Pro Pro
  180 185 190
Glu Arg Ile Arg Glu Lys Ser Arg Leu Phe Asp Thr Lys His Asp Val
195 200 205
Tyr Ser Phe Ala Ile Val Ile Trp Gly Val Leu Thr Gln Asn Asn Pro
 210 215
                          220
Phe Ala Asp Glu Lys Asn Ile Leu His Ile Met Met Lys Val Val Lys
225 230 235
Gly His Arg Pro Glu Leu Pro Pro Ile Cys Arg Pro Arg Pro Arg Ala 245 250 255
Cys Ala Ser Leu Ile Gly Leu Met Gln Arg Cys Trp His Ala Asp Pro
      260 265 270
Gln Val Arg Pro Thr Phe Gln Glu Ile Thr Ser Glu Thr Glu Asp Leu
 275 280 285
Cys Glu Lys Pro Asp Glu Glu Val Lys Asp Leu Ala His Glu Pro Gly
  290 295 300
Glu Lys Ser Ser Leu Glu Ser Lys Ser Glu Ala Arg Pro Glu Ser Ser
305 310 315 320
Arg Leu Lys Arg Ala Ser Ala Pro Pro Phe Asp Asn Asp Cys Ser Leu
      325 330 335
Ser Glu Leu Leu Ser Gln Leu Asp Ser Gly Ile Phe Pro Arg Leu Leu 340 345 350
Lys Gly Pro Glu Glu Leu Ser Arg Ser Ser Ser Glu Cys Lys Leu Pro 355 360 365
Ser Ser Ser Ser Gly Lys Arg Leu Ser Gly Val Ser Ser Val Asp Ser
 370 375
                               380
Asp Ala Ile Ile Ser Gly Asp Thr Ser Arg Leu Met Lys Ile Leu Gln
420 425 430
Pro Gln Asp Val Asp Leu Val Leu Asp Ser Ser Ala Ser Leu Leu His 435 440 440
Leu Ala Val Glu Ala Gly Gln Glu Glu Cys Val Lys Trp Leu Leu
 450 455 460
Asn Asn Ala Asn Pro Asn Leu Thr Asn Arg Lys Gly Ser Thr Pro Leu
            470 475
His Met Ala Val Glu Arg Lys Gly Arg Gly Ile Val Glu Leu Leu 485 490 495
Ala Arg Lys Thr Ser Val Asn Ala Lys Asp Glu Asp Gln Trp Thr Ala 500 505 510
Leu His Phe Ala Ala Gln Asn Gly Asp Glu Gly Gln His Lys Ala Ala
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Ala Arg Glu Glu Cys Phe Cys Gln
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    <211> 337
    <212> PRT
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<213> Rat

<220>

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Val Asp Glu Cys Ala Thr Asp Ser His Gln Cys Asn Pro Thr Gln Ile
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Cys Ile Asn Thr Glu Gly Gly Tyr Thr Cys Ser Cys Thr Asp Gly Tyr 35 40
Trp Leu Leu Glu Gly Gln Cys Leu Asp Ile Asp Glu Cys Arg Tyr Gly
50 55 60
Tyr Cys Gln Gln Leu Cys Ala Asn Val Pro Gly Ser Tyr Ser Cys Thr 65 70 75 80
Cys Asn Pro Gly Phe Thr Leu Asn Asp Asp Gly Arg Ser Cys Gln Asp 85 90 95
Val Asn Glu Cys Glu Thr Glu Asn Pro Cys Val Gln Thr Cys Val Asn
100 105 110
Thr Tyr Gly Ser Phe Ile Cys Arg Cys Asp Pro Gly Tyr Glu Leu Glu
115 120 125
Glu Asp Gly Ile His Cys Ser Asp Met Asp Glu Cys Ser Phe Ser Glu 130 140
Phe Leu Cys Gln His Glu Cys Val Asn Gln Pro Gly Ser Tyr Phe Cys 145 150 155 160
Ser Cys Pro Pro Gly Tyr Val Leu Leu Glu Asp Asn Arg Ser Cys Gln
      165 170 175
Asp Ile Asn Glu Cys Glu His Arg Asn His Thr Cys Thr Pro Leu Gln 180 185 190
Thr Cys Tyr Asn Leu Gln Gly Gly Phe Lys Cys Ile Asp Pro Ile Val
195 200 205
Cys Glu Glu Pro Tyr Leu Leu Ile Gly Asp Asn Arg Cys Met Cys Pro
210 215 220
Ala Glu Asn Thr Gly Cys Arg Asp Gln Pro Phe Thr Ile Leu Phe Arg 225 230 240
Asp Met Asp Val Val Ser Gly Arg Ser Val Pro Ala Asp Ile Phe Gln
245 250 255
Met Gln Ala Thr Thr Arg Tyr Pro Gly Ala Tyr Tyr Ile Phe Gln Ile
260 265 270
Lys Ser Gly Asn Glu Gly Arg Glu Phe Tyr Met Arg Gln Thr Gly Pro 275 280 285
Ile Ser Ala Thr Leu Val Met Thr Arg Pro Ile Lys Gly Pro Arg Asp
  290 295 300
Ile Gln Leu Asp Leu Glu Met Ile Thr Val Asn Thr Val Ile Asn Phe
305 310 315
Arg Gly Ser Ser Val Ile Arg Leu Arg Ile Tyr Val Ser Gln Tyr Pro
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Phe
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<211> 152

<212> PRT

<213> mouse

<400> 187

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Gln Gln Ser Asn Trp Thr Phe Asn Asn Thr Glu Ala Asp Tyr Ile Glu
     35 40
                              45
Glu Pro Val Ala Leu Lys Phe Ser His Pro Cys Leu Glu Asp His Asn
                    55
                                        60
Ser Tyr Cys Ile Asn Gly Ala Cys Ala Phe His His Glu Leu Lys Gln 65 70 . 75 80
Ala Ile Cys Arg Cys Phe Thr Gly Tyr Thr Gly Gln Arg Cys Glu His
85 90 95
Leu Thr Leu Thr Ser Tyr Ala Val Asp Ser Tyr Glu Lys Tyr Ile Ala
100 105 110
Ile Gly Ile Gly Val Gly Leu Leu Ile Ser Ala Phe Leu Ala Val Phe 115 120 125
Tyr Cys Tyr Ile Arg Lys Arg Cys Ile Asn Leu Lys Ser Pro Tyr Ile
130 135 140
                              140
Ile Cys Ser Gly Gly Ser Pro Leu
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     <211> 118
<212> PRT
     <213> Rat
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Leu Val Pro Gln Phe Gly Thr Arg Ile Arg Tyr ThrAla Tyr Asp Arg
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Ala Tyr Asn Arg Ala Ser Cys Lys Phe Ile Val Lys Val Gln Val Arg
20 25 30
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Arg Cys Pro Ile Leu Lys Pro Pro Gln His Gly Tyr Leu Thr Cys Ser 35
Ser Ala Gly Asp Asn Tyr Gly Ala Ile Cys Glu Tyr His Cys Asp Gly 50 60
Gly Tyr Glu Arg Gln Gly Thr Pro Ser Arg Val Cys Gln Ser Ser Arg
               70
                                   75
Gln Trp Ser Gly Ser Pro Pro Val Cys Thr Pro Met Lys Ile Asn Val
85 90 95
Asn Val Asn Ser Ala Ala Gly Leu Leu Asp Gln Phe Tyr Glu Lys Gln
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                                     110
Arg Leu Leu Ile Val Ser
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Leu Ala Ile Leu Cys Ser Leu Ala Leu Gly Ser Val Thr Val His
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                     25
Ser Ser Glu Pro Glu Val Arg Ile Pro Glu Asn Asn Pro Val Lys Leu
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40
Ser Cys Ala Tyr Ser Gly Phe Ser Ser Pro Arg Val Glu Trp Lys Phe 50 55 60
Asp Gln Gly Asp Thr Thr Arg Leu Val Cys Tyr Asn Asn Lys Ile Thr 65 70 75 80
Ala Ser Tyr Glu Asp Arg Val Thr Phe Leu Pro Thr Gly Ile Thr Phe
85 90 95
Lys Ser Val Thr Arg Glu Asp Thr Gly Thr Tyr Thr Cys Met Val Ser 100 105 110
Glu Glu Gly Gly Asn Ser Tyr Gly Glu Val Lys Val Lys Leu Ile Val
      115 120 125
Leu Val Pro Pro Ser Lys Pro Thr Val Asn Ile Pro Ser Ser Ala Thr
130 135 140
Ile Gly Asn Arg Ala Val Leu Thr Cys Ser Glu Gln Asp Gly Ser Pro 145 150 155 160
Pro Ser Glu Tyr Thr Trp Phe Lys Asp Gly Ile Val Met Pro Thr Asn
  165 170 175
Pro Lys Ser Thr Arg Ala Phe Ser Asn Ser Ser Tyr Val Leu Asn Pro
180 185 190
Thr Thr Gly Glu Leu Val Phe Asp Pro Leu Ser Ala Ser Asp Thr Gly 195 200 205
Glu Tyr Ser Cys Glu Ala Arg Asn Gly Tyr Gly Thr Pro Met Thr Ser
 210 215 220
Asn Ala Val Arg Met Glu Ala Val Glu Arg Asn Val Gly Val Ile Val
                                   235
              230
Ala Ala Val Leu Val Thr Leu Ile Leu Leu Gly Ile Leu Val Phe Gly 245 250 255
Ile Trp Phe Ala Tyr Ser Arg Gly His Phe Asp Arg Thr Lys Lys Gly 260 265 270
Thr Ser Ser Lys Lys Val Ile Tyr Ser Gln Pro Ser Ala Arg Ser Glu
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Gly Glu Phe Lys Gln Thr Ser Ser Phe Leu Val
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    <211> 91
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                            25
                                              30
Asn Trp Phe Leu Pro Ala Ser Arg Glu Ile Pro Glu His Ser Ala Leu
 35
                     40
Thr Arg Tyr Pro Ala Gln Ile Arg Gly Cys Trp Pro His Arg Leu Thr
 50 55
                             - -
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Lys Pro Gln Thr Cys Leu Pro Gln Ala Arg Ser Tyr Leu Ser His Glu
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                                  75
Val Thr Gln Ala Thr Arg Thr Cys Pro Gly Gly
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50 60 50 55 Pro Gln Asp Arg Phe Gly Lys Gly Cys Glu His Lys Cys Ala Cys Arg 65 70 75 80 Asn Gly Gly Leu Cys His Ala Thr Asn Gly Ser Cys Ser Cys Pro Leu 85 90 Gly Trp Met Gly Pro His Cys Glu His Ala Cys Pro Ala Gly Arg Tyr 100 105 110Gly Ala Ala Cys Leu Leu Glu Cys Ser Cys Gln Asn Asn Gly Ser Cys 115 120 125 Glu Pro Thr Ser Gly Ala Cys Leu Cys Gly Pro Gly Phe Tyr Gly Gln 130 135 140 140 Ala Cys Glu Asp Thr Cys Pro Ala Gly Phe His Gly Ser Gly Cys Gln 145 150 150 160 Arg Val Cys Glu Cys Gln Gln Gly Ala Pro Cys Asp Pro Val Ser Gly
165 170 175 Arg Cys Leu Cys Pro Ala Gly Phe Arg Gly Gln Phe Cys Glu Arg Gly 180 185 190 Cys Lys Pro Gly Phe Phe Gly Asp Gly Cys Leu Gln Gln Cys Asn Cys 195 200 205Pro Thr Gly Val Pro Cys Asp Pro Ile Ser Gly Leu Cys Leu Cys Pro 210 215 220 Pro Gly Arg Ala Gly Thr Thr Cys Asp Leu Asp Cys Arg Arg Gly Arg 230 235 240 Phe Gly Pro Gly Cys Ala Leu Arg Cys Asp Cys Gly Gly Gly Ala Asp 245 250 255 Cys Asp Pro Ile Ser Gly Gln Cys His Cys Val Asp Ser Tyr Thr Gly

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265
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                                                  270
Pro Thr Cys Arg Glu Val Pro Thr Gln Leu Ser Ser Ile Arg Pro Ala
 275 280
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Pro Gln His Ser Ser Ser Lys Ala Met Lys His
   290 295
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     <211> 314
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Lys Asn Leu Leu Pro Glu Thr Thr Tyr Arg Ile Arg Ile Gln Ala Ile
 35 40
Asn Glu Ile Gly Val Gly Pro Phe Ser Gln Phe Ile Lys Ala Lys Thr 50 55 60
Arg Pro Leu Pro Pro Ser Pro Pro Arg Leu Glu Cys Ala Ala Ser Gly 65 70 75 80
Pro Gln Ser Leu Lys Leu Lys Trp Gly Asp Ser Asn Ser Lys Thr His
85 90 95
Ala Ala Gly Asp Met Val Tyr Thr Leu Gln Leu Glu Asp Arg Asn Lys 100 105 110
Arg Phe Ile Ser Ile Tyr Arg Gly Pro Ser His Thr Tyr Lys Val Gln
115 120 125
Arg Leu Thr Glu Phe Thr Cys Tyr Ser Phe Arg Ile Gln Ala Met Ser 130 135 140
Glu Ala Gly Glu Gly Pro Tyr Ser Glu Thr Tyr Thr Phe Ser Thr Thr 145 150 155 160
Lys Ser Val Pro Pro Thr Leu Lys Ala Pro Arg Val Thr Gln Leu Glu
            165 170 175
Gly Asn Ser Cys Glu Ile Phe Trp Glu Thr Val Pro Pro Met Arg Gly
180 185 190
Asp Pro Val Ser Tyr Val Leu Gln Val Leu Val Gly Arg Asp Ser Glu
195 200 205
Tyr Lys Gln Val Tyr Lys Gly Glu Glu Ala Thr Phe Gln Ile Ser Gly 210 215 220
Leu Glm Ser Asn Thr Asp Tyr Arg Phe Arg Val Cys Ala Cys Arg Arg 225 230 235 240
225 230
Cys Val Asp Thr SerGln Glu Leu Ser Gly Ala Phe Ser Pro Ser Ala
245 250 255
Ala Phe Met Leu Gln Gln Arg Glu Val Met Leu Thr Gly Asp Leu Gly
         260 265 270
Gly Met Glu Glu Ala Lys Met Lys Gly Met Met Pro Thr Asp Glu Gln
     275 280
                                285
Phe Ala Ala Leu Ile Val Leu Gly Phe Ala Thr Leu Ser Ile Leu Phe
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                                 300
Ala Phe Ile Leu Gln Tyr Phe Leu Met Lys
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<213> mouse

<400> 195

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<210> 196 <211> 154

<212> PRT <213> Human

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<210> 197 <211> 171 <212> PRT

<213> Rat

<400> 197

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                                                                        120
ggagaccaca ggtgctaagt gagggtgctc acagaacccc ctcttcagcc agagatcact
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agcaggggaa ctgtggagaa ggcagccagc aaggaagagc ctgagagtag cctccatggg
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cttggagccc agctggtatc tgctgctctg tttggctgtc tctggggcag cagggactga
                                                                        300
ccctccaca gcgcccacca cagcagaaag acagcggcag cccacggaca tcatcttaga
                                                                        360
ctgcttcttg gtgacagaag acaggcaccg cggggctttt gccagcagtg gggacaggga
                                                                        420
gagggeettg ettgtgetga ageaggtace agtgetggat gatggeteee tggaaggeat
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ggcagtgacc tgcgagatct ccaagtattt cctccaggcc agacaagagg ccacttttga
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gaaagcacat tggttcatca gcaacatgca ggtttctaga ggtggcccca gtgtctccat
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ggtgatgaag actctaagag atgctgaagt tggagctgtc cggcacccta cactgaacct
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                                                                        960
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                                                                       1140
acttaacate etggeteece ecaaagtaca actgeacttg geaaacaagg atectetgee
                                                                       1200
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                                                                       1260
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                                                                       1320
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                                                                       1399
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      <211> 469
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      <213> Rat
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                                                                        120
agatatgcga gtgactctct tcaagcttct cctgctttgg ttggtgttaa gtctcctggg
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catecagety gegtgggggt tetacgggaa cacagtgace gggttgtate accgtecagg
                                                                        240
gaaatggcag caaatgaagc tctcaaaact cacagagaat aaaggaaggc agcaggagaa
                                                                        300
gggtetecag agatateget gggtetgetg geteetgtge tgtacettge tgetatecag
                                                                        360
acccettagg caactgcaga gggcttgggt tgggggactg gagtaccatg atgctcccag
                                                                        420
ggtgagcctc cactgccctc agccttgcct ccaacagcgt caggtactg
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      <211> 529
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                                                                        120
ccagacagac agtatgtgct gacagccttg gctgcgcggg ccaagcttag agcctggaat gatgtcgacg ccttgttcac cacaaagaac tggttgggtt acaccaagaa gagagcaccc
                                                                        180
                                                                        240
attggcttcc atcgagttgt ggaaattttg cacaagaaca gtgcccctgt ccagatattg
                                                                        300
caggaatatg tcaatctggt ggaagatgtg gacacaaagt tgaacttagc cactaagttc
                                                                        360
aagtgccatg atgttgtcat tgatacttgc cgagacctga aggatcgtca acagttgctt
                                                                        420
                                                                        480
gcatacagga gcaaagtaga taaaggatct gctgaggaag agaaaatcga tgtcatcctc
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ggcgcccgcc aggctgctac	cgagctgcgc	gctcttccag	gacctcatcc	gctacgggaa	180
gaccaagcag tccggctcgc					240
gtacttttct cacttctacg					300
gtctcagtct ctgttcctgg					360 420
tcttggggtc acgcagttcc					480
aggegagetg getetgteta gagaetette gagtgettet					540
gtactgtttc gggctggtct					600
catgaatgac aagaacgtgt					660
ccacatcttg ggaatgatga					720
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ctacatctcc atggctgtca					900
ctatgtcttc ttcagccaag	ccttgtctgc	gttcttcaac	cacaggttct	acaaaagcac	960
atttgtgtcc tacccaaagc					1020 1080
tatggtgaag agcgcagccc aagtacactt tctgcagctg					1140
acctcatccg ctacgggaag					1200
cggggatcc actagttcta			303000300	90009005	1230
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<210> 270 <211> 288 <212> DNA <213> Human	C.		·		
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tgcaagtgct cccggaaggg aagccaaagt acccgcactg aggtaccgag gtcaggagca aagtggtaca acgcctggaa	cgaggagaag ctgcctgcac	atggttatca cccaagctgc	tcaccaccaa agagcaccaa	gagcgtgtcc	120 180 240 288
<210> 271 <211> 234 <212> DNA <213> Mouse	`	•			
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<210> 272 <211> 234 <212> DNA <213> Human <400> 272			·		
tccaaatgca agtgctcccg gaaatgaagc caaagtaccc gtgtccaggt accgaggtca ttcatcaagt ggtacaacgc	gcactgcgag ggagcactgc	gagaagatgg ctgcacccca	ttatcatcac agctgcagag	caccaagagc caccaagcgc	120 180 234
<210> 273 <211> 645 <212> DNA <213> Mouse					
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atgctgtcgc tccgctcctt	gcttccacac	ctgggactgt	teetataeet	ggctctgcac	60
ttatcccct ccctctctgc					120
acctccgaca tcttggaaat					180
acagtgacgg tccccgtgaa	cgattcagtc	agtgccgtga	tcctgaaagc	agtgaaggag	240
gacgacagcc cagtgggcac	ctggagtgga	acatatgaga	agtgcaacga	cagcagtgtc	300
tactataact tgacatccca					360
tccgaggatg tgactaaagt					420
aagtcatccg tgaaaatgga					480
tctgagacca gccagaccat					540 600
aaggacacag ccaacaccac gtgaccacag ccaagaccac				taccacagec	645\
3-3	55 -		2		.,
<210> 274					
<211> 63	•			•	
<212> DNA <213> Mouse			* *		
<400> 274					
gggtacagtg atggttacca aac	agtgtgtagt	aggtteggaa	gcaaagtgcc	tcagtttctg	60 63
<210> 275					
<211> 388				-	
<212> PRT					
<213> Mouse		ı			

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Gly Ala Ala Gly Thr Asp Pro Pro Thr Ala Pro Thr Thr Ala Glu Arg
    20 25 30
Gln Arg Gln Pro Thr Asp Ile Ile Leu Asp Cys Phe Leu Val Thr Glu
35 40 45
Asp Arg His Arg Gly Ala Phè Ala Ser Ser Gly Asp Arg Glu Arg Ala
50 60
       55
                                    60
Leu Leu Val Leu Lys Gln Val Pro Val Leu Asp Asp Gly Ser Leu Glu
65 70
                        75
Gly Ile Thr Asp Phe Gln Gly Ser Thr Glu Thr Lys Gln Asp Ser Pro
85 90 95
Val Ile Phe Glu Ala Ser Val Asp Leu Val Gln Ile Pro Gln Ala Glu
100 105 110
Ala Leu Leu His Ala Asp Cys Ser Gly Lys Ala Val Thr Cys Glu Ile
 115 120
                                     125
Ser Lys Tyr Phe Leu Gln Ala Arg Gln Glu Ala Thr Phe Glu Lys Ala
          135
                            1.40
His Trp Phe Ile Ser Asn Met Gln Val Ser Arg Gly Gly Pro Ser Val 145 150 150 155 160
Ser Met Val Met Lys Thr Leu Arg Asp Ala Glu Val Gly Ala Val Arg
   165 170 175
His Pro Thr Leu Asn Leu Pro Leu Ser Ala Gln Gly Thr Val Lys Thr
         180 185
                                          190
Gln Val Glu Phe Gln Val Thr Ser Glu Thr Gln Thr Leu Asn His Leu
    195 200
                               205
Leu Gly Ser Ser Val Ser Leu His Cys Ser Phe Ser Met Ala Pro Asp 210 215 220
Leu Asp Leu Thr Gly Val Glu Trp Arg Leu Gln His Lys Gly Ser Gly
225 230 235
Gly Ala Thr Leu Glu Pro Glu Glu Leu Leu Arg Ala Gly Asn Ala Ser
260 265 270
Leu Thr Leu Pro Asn Leu Thr Leu Lys Asp Glu Gly Thr Tyr Ile Cys 275 280 285
Gln Ile Ser Thr Ser Leu Tyr Gln Ala Gln Gln Ile Met Pro Leu Asn
 290 295 300
Ile Leu Ala Pro Pro Lys Val Gln Leu His Leu Ala Asn Lys Asp Pro 305 310 315 320
Leu Pro Ser Leu Val Cys Ser Ile Ala Gly Tyr Tyr Pro Leu Asp Val 325 330 335
Gly Val Thr Trp Ile Arg Glu Glu Leu Gly Gly Ile Pro Ala Gln Val
      340 345 350
Ser Gly Ala Ser Phe Ser Ser Leu Arg Gln Ser Thr Met Gly Thr Tyr
     355 360
Ser Ile Ser Ser Thr Val Met Ala Asp Pro Gly Pro Thr Gly Ala Thr
                                   380
 370
                 375
Tyr Thr Cys Gln
385
     <210> 276
     <211> 151
     <212> PRT
     <213> Rat
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<400> 276 Met Ala Glu Pro Trp Ala Gly Gln Phe Leu Gln Ala Leu Pro Ala Thr 10 Val Leu Gly Ala Leu Gly Thr Leu Gly Ser Glu Phe Leu Arg Glu Trp 20 25 30 Glu Thr Gln Asp Met Arg Val Thr Leu Phe Lys Leu Leu Leu Trp 40 35 45 Leu Val Leu Ser Leu Leu Gly Ile Gln Leu Ala Trp Gly Phe Tyr Gly 55 Asn Thr Val Thr Gly Leu Tyr His Arg Pro Gly Lys Trp Gln Gln Met 65 70 75 80 Lys Leu Ser Lys Leu Thr Glu Asn Lys Gly Arg Gln Gln Glu Lys Gly 85 90 Leu Gln Arg Tyr Arg Trp Val Cys Trp Leu Leu Cys Cys Thr Leu Leu 105 100 110 Leu Ser Arg Pro Leu Arg Gln Leu Gln Arg Ala Trp Val Gly Gly Leu 120 115 125 Glu Tyr His Asp Ala Pro Arg Val Ser Leu His Cys Pro Gln Pro Cys 130 135 140 Leu Gln Gln Arg Gln Val Leu 145

<210> 277 <211> 163 <212> PRT

<213> Rat

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> <210> 278 <211> 330 <212> PRT <213> Rat

Trp Lys Asn

<400> 278



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Met Ala Gly Trp Ala Gly Ala Glu Leu Ser Val Leu Asn Pro Leu Arg
Ala Leu Trp Leu Leu Leu Ala Ala Phe Leu Leu Ala Leu Leu
                              25
Gln Leu Ala Pro Ala Arg Leu Leu Pro Ser Cys Ala Leu Phe Gln Asp
                        40
      35
Leu Ile Arg Tyr Gly Lys Thr Lys Gln Ser Gly Ser Arg Arg Pro Ala
                     55`
                                         60
   50
Val Cys Arg Ala Phe Asp Val Pro Lys Arg Tyr Phe Ser His Phe Tyr
                 70
                                    75
Val Val Ser Val Leu Trp Asn Gly Ser Leu Leu Trp Phe Leu Ser Gln
85 90 95
                               90
Ser Leu Phe Leu Gly Ala Pro Phe Pro Ser Trp Leu Trp Ala Leu Leu
         100
                            105
                                                110
Arg Thr Leu Gly Val Thr Gln Phe Gln Ala Leu Gly Met Glu Ser Lys
                         120
     115
Ala Ser Arg Ile Gln Ala Gly Glu Leu Ala Leu Ser Thr Phe Leu Val
            135
                                      140
Leu Val Phe Leu Trp Val His Ser Leu Arg Arg Leu Phe Glu Cys Phe
                 150
                                     155
Tyr Val Ser Val Phe Ser Asn Thr Ala Ile His Val Val Gln Tyr Cys
             165
                               170
Phe Gly Leu Val Tyr Tyr Val Leu Val Gly Leu Thr Val Leu Ser Gln
                              185
           180
                                                190
Val Pro Met Asn Asp Lys Asn Val Tyr Ala Leu Gly Lys Asn Leu Leu
                         200
      195
                                            205
Leu Gln Ala Arg Trp Phe His Ile Leu Gly Met Met Phe Phe Trp
                   215
                                       220
   210
Ser Ser Ala His Gln Tyr Lys Cys His Val Ile Leu Ser Asn Leu Arg
                230
                                   235
Arg Asn Lys Lys Gly Val Val Ile His Cys Gln His Arg Ile Pro Phe
             245
                        250 .
Gly Asp Trp Phe Glu Tyr Val Ser Ser Ala Asn Tyr Leu Ala Glu Leu
                             265
                                              270
          260
Met Ile Tyr Ile Ser Met Ala Val Thr Phe Gly Leu His Asn Val Thr 275 280 285
                       280
                                            285
Trp Trp Leu Val Val Thr Tyr Val Phe Phe Ser Gln Ala Leu Ser Ala
                   295
                                300
Phe Phe Asn His Arg Phe Tyr Lys Ser Thr Phe Val Ser Tyr Pro Lys 305 310 315 320
His Arg Lys Ala Phe Leu Pro Phe Leu Phe
              325
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<210> 279 <211> 61 <212> PRT <213> Rat

<400> 279

 Met Glu Asn Ile Tyr Tyr Thr Asn Leu Ile Thr Ile Leu Gly Asn Lys

 1
 5
 10
 15

 His Ala Asn Gln Met Glu Leu Asn Leu Gln Ala Leu Ile Leu Ser Pro 20
 25
 30

 Trp Phe Ala Val Cys Ala Pro Pro Gly Phe Ala Arg Asp Gln Ala Val 35
 40
 45

 Arg Gly Leu Ala Leu Ala Gly Arg Arg Ile Thr Val Val 50
 55
 60

<210> 280 <211> 105 <212> PRT <213> Rat <400> 280 Met Leu Arg Arg Gln Leu Val Trp Trp His Leu Leu Ala Leu Leu Phe 10 Leu Pro Phe Cys Leu Cys Gln Asp Glu Tyr Met Glu Ser Pro Gln Ala 20 25 Gly Gly Leu Pro Pro Asp Cys Ser Lys Cys Cys His Gly Asp Tyr Gly 35 40 45 Phe Arg Gly Tyr Gln Gly Pro Pro Gly Pro Pro Gly Pro Pro Gly Ile 55 50 60 Pro Gly Asn His Gly Asn Asn Gly Asn Asn Gly Ala Thr Gly His Glu 70 75 Gly Ala Lys Gly Glu Lys Gly Asp Lys Gly Asp Leu Gly Pro Arg Gly 90 85 Glu Arg Gly Gln His Gly Pro Lys Gly 100 <210> 281 <211> 27 <212> PRT <213> Mouse <400> 281 Met Leu Lys Ala Ser Leu His Ile Leu Phe Leu Gly Ile Leu Asn Val 1 5 10 10 15 Pro Ile Val Asp Thr Ser Thr Lys Thr Gly Val 20 <210> 282 <211> 169 <212> PRT <213> Mouse <400> 282 Met Ser Gly Leu Arg Thr Leu Leu Gly Leu Gly Leu Leu Val Ala Gly 10 Ser Arg Leu Pro Arg Val Ile Ser Gln Gln Ser Val Cys Arg Ala Arg 20 25 30 Pro Ile Trp Trp Gly Thr Gln Arg Arg Gly Ser Glu Thr Met Ala Gly 40 Ala Ala Val Lys Tyr Leu Ser Gln Glu Glu Ala Gln Ala Val Asp Gln 55 60

Glu Leu Phe Asn Glu Tyr Gln Phe Ser Val Asp Gln Leu Met Glu Leu

Ala Gly Leu Ser Cys Ala Thr Ala Ile Ala Lys Ala Tyr Pro Pro Thr

Ser Met Ser Lys Ser Pro Pro Thr Val Leu Val Ile Cys Gly Pro Gly

Asn Asn Gly Gly Asp Gly Leu Val Cys Ala Arg His Leu Lys Leu Phe

Gly Tyr Gln Pro Thr Ile Tyr Tyr Pro Lys Arg Pro Asn Lys Pro Leu

120

135

105

70

100

115

130

85

75

110

125



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Phe Thr Gly Leu Val Thr Gln Cys Gln Lys Met Asp Ile Pro Phe Leu
145
                 150
                                    155
Gly Glu Met Pro Pro Glu Asp Gly Met
             165
     <210> 283
     <211> 61
     <212> PRT
     <213> Mouse
     <400> 283
Met Glu Lys Gln Met Asp Ala Ser Val Ser Val Ile Phe Gly Ser Ile
         5
 1
                              1.0
Val Ile Ser Ala Phe Leu Tyr Leu Ser Leu Ala Gly Pro Trp Ala Val
        20
                            25
                                             30
Thr Val Thr Gln Met Arg Thr Ile Ile Ile Thr Met Asp Gln Leu Arg
     35
                        40
Asp Ala Leu Ile Leu Asp Gln Leu Lys Val Ala Val Ser
   50
                      55
     <210> 284
     <211> 131
     <212> PRT
     <213> Mouse
     <400> 284
Met Ala Pro Ser Leu Trp Lys Gly Leu Val Gly Val Gly Leu Phe Ala
 1
                                 10
Leu Ala His Ala Ala Phe Ser Ala Ala Gln His Arg Ser Tyr Met Arg
    20
                             25
Leu Thr Glu Lys Glu Asp Glu Ser Leu Pro Ile Asp Ile Val Leu Gln
 35
                         40
                                           45
Thr Leu Leu Ala Phe Ala Val Thr Cys Tyr Gly Ile Val His Ile Ala
   50
                   55
                                       60
Gly Glu Phe Lys Asp Met Asp Ala Thr Ser Glu Leu Lys Asn Lys Thr
                70
                                   75
Phe Asp Thr Leu Arg Asn His Pro Ser Phe Tyr Val Phe Asn His Arg
            85
                              90
Gly Arg Val Leu Phe Arg Pro Ser Asp Ala Thr Asn Ser Ser Asn Leu
                           105
        100
                                             110
Asp Ala Leu Ser Ser Asn Thr Ser Leu Lys Leu Arg Lys Phe Asp Ser
    115
                       120
                                            125
Leu Arg Arg
   130
     <210> 285
     <211> 78
     <212> PRT
     <213> Mouse
     <400> 285
Gly Thr Arg Lys Pro Leu Pro Met Glu Ala His Ser Arg Arg Glu Lys
                                 10
                                                   15
Ala Ser Gly Leu Arg Leu Ala Trp His Tyr Glu Cys Ser Gly Val Ser
                            25
        20
                                             30
Val Trp Trp Met Cys Val Leu Gly Trp Leu Ser Phe Leu Val Phe Leu
       35
                         40
                                           45
```



<210> 286 <211> 206 <212> PRT <213> Mouse

<400> 286

Met Leu Pro Pro Ala Ile His Leu Ser Leu Ile Pro Leu Leu Cys Ile 1 Leu Met Arg Asn Cys Leu Ala Phe Lys Asn Asp Ala Thr Glu Ile Leu 20 25 30 Tyr Ser His Val Val Lys Pro Val Pro Ala His Pro Ser Ser Asn Ser 35 40 45 Thr Leu Asn Gln Ala Arg Asn Gly Gly Arg His Phe Ser Ser Thr Gly 55 60 Leu Asp Arg Asn Ser Arg Val Gln Val Gly Cys Arg Glu Leu Arg Ser 70 75 Thr Lys Tyr Ile Ser Asp Gly Gln Cys Thr Ser Ile Ser Pro Leu Lys 90 85 Glu Leu Val Cys Ala Gly Glu Cys Leu Pro Leu Pro Val Leu Pro Asn 100 105 110 105 110 100 Trp Ile Gly Gly Gly Tyr Gly Thr Lys Tyr Trp Ser Arg Arg Ser Ser 120 115 Gln Glu Trp Arg Cys Val Asn Asp Lys Thr Arg Thr Gln Arg Ile Gln 130 135 140 Leu Gln Cys Gln Asp Gly Ser Thr Arg Thr Tyr Lys Ile Thr Val Val 145 150 155 160 155 Thr Ala Cys Lys Cys Lys Arg Tyr Thr Arg Gln His Asn Glu Ser Ser . 165 170 His Asn Phe Glu Ser Val Ser Pro Ala Lys Pro Ala Gln His His Arg 185 180 Glu Arg Lys Arg Ala Ser Lys Ser Ser Lys His Ser Leu Ser 195 200

<210> 287 <211> 169 <212> PRT <213> Mouse

<400> 287

Met Ser Gly Leu Arg Thr Leu Leu Gly Leu Gly Leu Leu Val Ala Gly 15 10 Ser Arg Leu Pro Arg Val Ile Ser Gln Gln Ser Val Cys Arg Ala Arg 20 . 25 30 Pro Ile Trp Trp Gly Thr Gln Arg Arg Gly Ser Glu Thr Met Ala Gly 35 40 45 .Ala Ala Val Lys Tyr Leu Ser Gln Glu Glu Ala Gln Ala Val Asp Gln 55 Glu Leu Phe Asn Glu Tyr Gln Phe Ser Val Asp Gln Leu Met Glu Leu 75 70 Ala Gly Leu Ser Cys Ala Thr Ala Ile Ala Lys Ala Tyr Pro Pro Thr 90 95 85 Ser Met Ser Lys Ser Pro Pro Thr Val Leu Val Ile Cys Gly Pro Gly

<210> 288 <211> 114 <212> PRT <213> Mouse

<400> 288

Met Ser Val Thr Ile Gly Arg Leu Ala Leu Phe Leu Ile Gly Ile Leu 10 Leu Cys Pro Val Ala Pro Ser Leu Thr Arg Ser Trp Pro Gly Pro Asp 20 25 30 Thr Cys Ser Leu Phe Leu Gln His Ser Leu Ser Leu Ser Leu Arg Leu 35 40 45 Gly Gln Ser Leu Glu Gly Gly Leu Ser Val Cys Phe His Val Cys Ile 55 60 His Ala Cys Glu Cys Val Ala Cys Cys Arg Val Leu Trp Asp Pro Lys 70 75 Pro Arg Gly Ser Ser Leu Cys Arg Trp Val Leu Gly Ser Ile Thr Cys 90 85 Leu Phe Met Tyr Glu Val Gly Gly Trp Thr Gln Gly Gly Leu Ile Val 105 100 Ser Leu

<210> 289 <211> 46 <212> PRT <213> Mouse

40

<210> 290 <211> 199 <212> PRT <213> Mouse

35

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Gly Phe Cys Gln Leu Ser Gln Leu Ala Ser Ala Asp Pro Glu Arg Arg
                                                               55
Ser Pro Arg Ala Ile Val Pro Arg Ala Pro Arg Pro Arg Ser Arg Arg
                                                                                                          75
                                                   70
Arg Pro Cys Leu Pro Gly Phe Ser Arg Arg Phe Pro Arg Glu Arg Arg
                                                                                                     90
                                          85
Ser Pro Gly Gln Pro Pro Ser Arg Thr Pro Gln Pro Pro Gln Pro Cys
Arg Gly Pro Ser Pro Gly Thr Ala Gln Thr Arg Ser Asn Leu Arg Gly
                                                  120
 Trp Gln Arg Gly Gly Ser Ile Val Leu Gln Ala Ser Glu Arg Thr Arg
        130
                                                           135
                                                                                                                           140
Ala Gly Cys Arg Thr Pro Val Cys Val Ser His Pro Ser Ala Phe Pro
                                                                                                              155
                                                 150
Pro Pro Arg Ala Leu Phe Gly Val Phe Val Ala Ser Ala Pro Glu Val
165 170 175
Val Cys Val Cys Val Ser Val Leu Ser Val Cys Leu Leu Ser Pro
                                                                                          185
                               180
Arg Gly Lys Thr Leu Val Asp
                     195
                  <210> 291
                 <211> 568
                  <212> PRT
                  <213> Rat
                  <400> 291
Met Glu Leu Leu Tyr Trp Cys Leu Leu Cys Leu Leu Leu Pro Leu Thr 1 \hspace{1cm} 
                                               5
 Ser Arg Thr Gln Lys Leu Pro Thr Arg Asp Glu Glu Leu Phe Gln Met
                           20
                                                                                          25
 Gln Ile Arg Asp Lys Ala Leu Phe His Asp Ser Ser Val Ile Pro Asp
                                                                      40
 Gly Ala Glu Ile Ser Ser Tyr Leu Phe Arg Asp Thr Pro Arg Arg Tyr
                                                              55
                                                                                                                 60
 Phe Phe Met Val Glu Glu Asp Asn Thr Pro Leu Ser Val Thr Val Thr
                                                        70
                                                                                                                75
 Pro Cys Asp Ala Pro Leu Glu Trp Lys Leu Ser Leu Gln Glu Leu Pro
                                       85 -
                                                                                                   90
 Glu Glu Ser Ser Ala Asp Gly Ser Gly Asp Pro Glu Pro Leu Asp Gln
                                                                                        105
                                                                                                                                                 110
 Gln Lys Gln Gln Met Thr Asp Val Glu Gly Thr Glu Leu Phe Ser Tyr
                                                                              1.20
                     115
                                                                                                                                        125
 Lys Gly Asn Asp Val Glu Tyr Phe Leu Ser Ser Ser Ser Pro Ser Gly 130 140
                                                             135
                                                                                                                      140
Leu Tyr Gln Leu Glu Leu Leu Ser Thr Glu Lys Asp Thr His Phe Lys
145 150 155 160
                                                         150
                                                                                                               155
 Val Tyr Ala Thr Thr Thr Pro Glu Ser Asp Gln Pro Tyr Pro Asp Leu
165 170 . 175
 Pro Tyr Asp Pro Arg Val Asp Val Thr Ser Ile Gly Arg Thr Thr Val
 Thr Leu Ala Trp Lys Gln Ser Pro Thr Ala Ser Met Leu Lys Gln Pro
 Ile Glu Tyr Cys Val Val Ile Asn Lys Glu His Asn Phe Lys Ser Leu
                                                                                                                220
                                                             215
```

Cys Ala Ala Glu Thr Lys Met Ser Ala Asp Asp Ala Phe Met Val Ala

```
230
                                    235
Pro Lys Pro Gly Leu Asp Phe Ser Pro Phe Asp Phe Ala His Phe Gly
                             250
              245
                                                   255
Phe Pro Thr Asp Asn Leu Gly Lys Asp Arg Ser Phe Leu Ala Lys Pro
          260
                            265
                                            270
Ser Pro Lys Val Gly Arg His Val Tyr Trp Arg Pro Lys Val Asp Ile
    275 280
                                          285
Lys Lys Ile Cys Ile Gly Ser Lys Asn Ile Phe Thr Val Ser Asp Leu
                     295
                                       300
Lys Pro Asn Thr Gln Tyr Tyr Phe Asp Val Phe Met Val Asn Thr Asn
305
                 310
                                    315
Thr Asn Met Asn Thr Ala Phe Val Gly Ala Phe Ala Arg Thr Lys Glu
                                                335
             325
                              330
Glu Ala Lys Gln Lys Thr Val Glu Leu Lys Asp Gly Arg Val Thr Asp
                           345
          340
Val Val Val Lys Arg Lys Gly Lys Lys Phe Leu Arg Phe Ala Pro Val 355 360 365
                                           365
Ser Ser His Gln Lys Val Thr Leu Phe Ile His Ser Cys Met Asp Thr
                              380
   370
                  375
Val Gln Val Gln Val Arg Arg Asp Gly Lys Leu Leu Ser Gln Asn
                 390
                                    395
Val Glu Gly Ile Arg Gln Phe Gln Leu Arg Gly Lys Pro Lys Gly Lys
              405
                                410
Tyr Leu Ile Arg Leu Lys Gly Asn Lys Lys Gly Ala Ser Met Leu Lys
               425
          420
Ile Leu Ala Thr Thr Arg Pro Ser Lys His Ala Phe Pro Ser Leu Pro
                       440
     435
                                          445
Asp Asp Thr Arg Ile Lys Ala Phe Asp Lys Leu Arg Thr Cys Ser Ser
                   455
                                      460
Val Thr Val Ala Trp Leu Gly Thr Gln Glu Arg Arg Lys Phe Cys Ile
465 470 475 480
                 470
                                  475
Tyr Arg Lys Glu Val Gly Gly Asn Tyr Ser Glu Glu Gln Lys Arg Arg
             485
                                490
                                                   495
Glu Arg Asn Gln Cys Leu Gly Pro Asp Thr Arg Lys Lys Ser Glu Lys 500 505 510
Val Leu Cys Lys Tyr Phe His Ser Gln Asn Leu Gln Lys Ala Val Thr
                                  525
                        520
       515
Thr Glu Thr Ile Arg Asp Leu Gln Pro Gly Lys Ser Tyr Leu Leu Asp
                     535
                                        540
   530
Val Tyr Val Val Gly His Gly Gly His Ser Val Lys Tyr Gln Ser Lys
       550
                                   555
                                                       560
Leu Val Lys Thr Arg Lys Val Cys
              565
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<210> 292 <211> 123 <212> PRT

<213> Mouse

<400> 292

 Met
 Leu
 Thr
 Glu
 Pro
 Ala
 Gln
 Leu
 Phe
 Val
 His
 Lys
 Asn
 Gln
 Pro

 Pro
 Ser
 His
 Ser
 Leu
 Arg
 Leu
 His
 Phe
 Arg
 Thr
 Leu
 Ala
 Gly
 Ala

 Leu
 Ala
 Leu
 Ser
 Ser
 Thr
 Gln
 Met
 Ser
 Trp
 Gly
 Leu
 Gln
 Ile
 Leu
 Pro

 Cys
 Leu
 Ser
 Leu
 Leu
 Leu
 Leu
 Trp
 Asn
 Gln
 Val
 Pro
 Gly
 Leu
 Glu
 Leu
 Glu
 Glu
 Leu
 Glu
 Leu
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 Glu
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 Asn
 Gln
 Val
 Pro
 Gly
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 Leu
 Leu
 Leu
 Trp
 Asn
 Gln
 Val
 Pro
 Gly
 Leu
 Glu
 Leu
 Leu
 Leu
 Trp
 Asn

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55
Gly Gln Glu Phe Arg Phe Gly Ser Cys Gln Val Thr Gly Val Val Leu
                   70
Pro Glu Leu Trp Glu Ala Phe Trp Thr Val Lys Asn Thr Val Gln Thr 85 90 95
              85
Gln Asp Asp Ile Thr Ser Ile Arg Leu Leu Lys Pro Gln Val Leu Arg
        100 · 105
Asn Val Ser Val Ile Arg Tro Glu Gly Asp Ser
      115 120
      <210> 293
      <211> 66
      <212> PRT
      <213> Mouse
     <400> 293
Met Asp Val Trp Ser Gly Leu Pro Leu Glu Thr Leu Trp Ile Tyr Glu 1 5 5 10 10 10
Ala Val Leu Pro Trp Leu Leu Met Gly Gln Gly His Ala Trp Val Cys
         20
                              25
Gly Pro Ile Ala Leu Trp Val Phe Val Asn Val Pro Gly Leu Cys Tyr
    35
                       40
                                              45
His Gln Lys Pro Phe Arg Cys Pro Trp Ser Gly Leu Leu Pro Glu Ala
                        55
   50
Leu Cys
      <210> 294
      <211> 294
      <212> PRT
      <213> Rat
     <400> 294
Met Thr Val Phe Arg Lys Val Thr Thr Met Ile Ser Trp Met Leu Leu
                                    10
Ala Cys Ala Leu Pro Cys Ala Ala Asp Pro Met Leu Gly Ala Phe Ala 20 25 30
     20
                               25
                                                    30
Arg Arg Asp Phe Gln Lys Gly Gly Pro Gln Leu Val Cys Ser Leu Pro
                          40
Gly Pro Gln Gly Pro Pro Gly Pro Pro Gly Ala Pro Gly Ser Ser Gly
                     55
                                         60
Met Val Gly Arg Met Gly Phe Pro Gly Lys Asp Gly Gln Asp Gly Gln
                                       75
                   70
Asp Gly Asp Arg Gly Asp Ser Gly Glu Glu Gly Pro Pro Gly Arg Thr
                                 90
              85
Gly Asn Arg Gly Lys Gln Gly Pro Lys Gly Lys Ala Gly Ala Ile Gly 100 105 ... 110
Arg Ala Gly Pro Arg Gly Pro Lys Gly Val Ser Gly Thr Pro Gly Lys 115 \phantom{\bigg|}^{\phantom{}} 120 \phantom{\bigg|} 125
His Gly Ile Pro Gly Lys Lys Gly Pro Lys Gly Lys Lys Gly Glu Pro 130 \phantom{\bigg|} . 135 \phantom{\bigg|} 140
Gly Leu Pro Gly Pro Cys Ser Cys Gly Ser Ser Arg Ala Lys Ser Ala
                                        155 ·
                   150
Phe Ser Val Ala Val Thr Lys Ser Tyr Pro Arg Glu Arg Leu Pro Ile
               165
                                   170
                                                     175
Lys Phe Asp Lys Ile Leu Met Asn Glu Gly Gly His Tyr Asn Ala Ser
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Ser Gly Lys Phe Val Cys Ser Val Pro Gly Ile Tyr Tyr Phe Thr Tyr 200 195 205 Asp Ile Thr Leu Ala Asn Lys His Leu Ala Ile Gly Leu Val His Asn 215 210 220 Gly Gln Tyr Arg Ile Arg Thr Phe Asp Ala Asn Thr Gly Asn His Asp 230 225 235 Val Ala Ser Gly Ser Thr Ile Leu Ala Leu Lys Glu Gly Asp Glu Val 245 250 255 245 Trp Leu Gln Ile Phe Tyr Ser Glu Gln Asn Gly Leu Phe Tyr Asp Pro 260 265 270 Tyr Trp Thr Asp Ser Leu Phe Thr Gly Phe Leu Ile Tyr Ala Asp Gln 280 275 Gly Asp Pro Asn Glu Val 290

<210> 295 <211> 243 <212> PRT , <213> Rat

<400> 295

Met Arg Pro Leu Leu Ala Leu Leu Leu Gly Leu Ala Ser Gly Ser 10 15 Pro Pro Leu Asp Asp Asn Lys Ile Pro Ser Leu Cys Pro Gly Gln Pro 20 25 30Gly Leu Pro Gly Thr Pro Gly His His Gly Ser Gln Gly Leu Pro Gly 35 40 45 Arg Asp Gly Arg Asp Gly Arg Asp Gly Ala Pro Gly Ala Pro Gly Glu 50 60 55 Lys Gly Glu Gly Arg Pro Gly Leu Pro Gly Pro Arg Gly Glu Pro 65 70 75 80 75 70 Gly Pro Arg Gly Glu Ala Gly Pro Val Gly Ala Ile Gly Pro Ala Gly 85 90 95 Glu Cys Ser Val Pro Pro Arg Ser Ala Phe Ser Ala Lys Arg Ser Glu 100 105 110 Ser Arg Val Pro Pro Pro Ala Asp Thr Pro Leu Pro Phe Asp Arg Val 115 120 125 115 120 Leu Leu Asn Glu Gln Gly His Tyr Asp Ala Thr Thr Gly Lys Phe Thr 135 140 Cys Gln Val Pro Gly Val Tyr Tyr Phe Ala Val His Ala Thr Val Tyr 145 150 160 Arg Ala Ser Leu Gln Phe Asp Leu Val Lys Asn Gly Gln Ser Ile Ala 165 170 175Ser Phe Phe Gln Phe Phe Gly Gly Trp Pro Lys Pro Ala Ser Leu Ser 185 180 Gly Gly Ala Met Val Arg Leu Glu Pro Glu Asp Gln Vál Trp Val Gln 195 200 205 · Val Gly Val Gly Asp Tyr Ile Gly Ile Tyr Ala Ser Ile Lys Thr Asp 210 215 220 Ser Thr Phe Ser Gly Phe Leu Val Tŷr Ser Asp Trp His Ser Ser Pro 225 235 230

<210> 296 <211> 444 <212> PRT

Val Phe Ala



<213> Rat

		100>													
Met 1	Leu	Val	Ala	Phe 5	Leu	Gly	Ala	Ser	Ala 10	Val	Thr	Ala	Ser	Thr 15	Gly
			20			His		25					30		
		35				Asp	40					45			
Val	Ser 50	Ser	His	Glu	Gly	Ser 55	Ala	Ala	Asp	Thr	Ala 60	Ala	Glu	Pro	Tyr
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				85		Ile			90					95	Ile
Phe	Arg	Tyr	Phe 100	Ala	Thr	Leu	Lys	Val 105	Ile	Asn	Glu	Pro	Gly 110	Glu	Thr
		115				Gln	120					125			
Glu	Lys 130	Gln	Pro	Glu	His	Leu 135	Gly	Leu	Asp	Gln	Tyr 140	Ile	Ile	Lys	Arg
Phe 145	Asp	Gly	Lys	Lys	Ile 150	Ala	Gln	Glu	Arg	Glu 155	Lys	Phe	Ala	Asp	Glu 160
Gly	Ser	Ile	Phe	Tyr 165	Thr	Leu	Gly	Gļu	Cys 170	Gly	Leu	Ile	Ser	Phe 175	Ser
Asp	Tyr	Ile	Phe 180	Leu	Thr	Thr	Val	Leu 185	Ser	Thr	Pro	Gln	Arg 190	Asn	Phe
Glu	Ile	Ala 195	Phe	Lys	Met	Phe	Asp 200	Leu	Asn	Gly	Asp	Gly 205	Glu	Val	Asp
Met	Glu 210		Phe	Glu	Gln	Val 215	Gln	Ser	Ile	Ile	Arg 220	Ser	Gln	Thr	Ser
Met 225	Gly	Met	Arg	His	Arg 230	qaA	Arg	Pro	Thr	Thr 235	G1y	Asn	Thr	Leu	Lys 240
Ser	Gly	Leu	Cys	Ser 245	Ala	Leu	Thr	Thr	Tyr 250	Phe	Phe	Gly	Ala	Asp 255	Leu
			260			Lys		265					270	_	
		275				Leu	280					285			
Gly	Arg 290	Ile	Ser	Glu	Arg	Gln 295	Phe	Gly	Gly	Met	Leu 300	Leu	Ala	Tyr	Ser
Gly 305	Val	Gln	Ser	Lys	Lys 310	Leu	Thr	Ala	Met	Gln 315	Arg	Gln	Leu	Lys,	Lys 320
His	Phe	Lys	Asp	Gly 325	Lys	Gly	Leu	Thr	Phe 330	Gln	Glu	Val	Glu	Asn 335	Phe
Phe	Thr	Phe	Leu 340	Lys	Asn	Ile	Asn	Asp 345	Val	Asp	Thr		Leu 350	Ser	Phe
Tyr	His	Met 355	Ala	Gly	Ala	Ser	Leu 360	Asp	Lys	Val	Thr	Met 365	Gln	Gln	Val
Ala	Arg 370	Thr	Val	Ala	Lys	Val 375	Glu	Leu	Ser	Asp	His 380	Val	Cys	Asp	Val
Val 385	Phe	Ala	Leu	Phe	Asp 390	Cys	Asp	Gly	Asn	Gly 395	Glu	Leu	Ser	Asn	Lys 400
Glu	Phe	Val	Ser	Ile 405	Met	Lys	Gln	Arg	Leu 410	Met	Arg	Gly	Leu	Glu 415	Lys
Pro	Lys	Asp	Met 420	Gly	Phe	Thr	Arg	Leu 425	Met	Gln	Ala	Met	Trp 430	Lys	Cys

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Trp Ala Asp Tyr Leu Arg Arg Val Ala Pro Thr Ala Leu Ala Thr Ala
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Ile Val Pro Thr Glu Ser Ser Tyr Arg Ser Pro Ser Phe Leu Ala Gly
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Phe	Arg	Phe 35		Cys	Ser	Pro	Trp		Gln	His	Phe	Gly 45		Gly	Arg
Leu	Thr 50	Ser	Cys	Leu	Pro	Pro 55	Cys	Val	Asp	Arg	Val 60	Val	Lys	Thr	Tyr
Ser 65	-	Pro	Pro		Leu ,70		Val	Asn	Gly	His 75		Val	Thr	Ile	Суs 80
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			20					25					30	Cys	
Ala	Thr	Leu 35	Leu	Pro	Leu	Leu	Phe 40	Leu	Leu	Pro	His	Leu 45	His	Ser	Thr
Leu	Ser 50	Arg	Val	Gln	Arg	Leu 55	Asn	Phe	Asn	Ile	Gly 60	His	Leu	Gly	Val
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Ala	Ser	Lys 35	Thr	Leu	Leu	Glu	Lys 40	Thr	Gln	Phe	Ser	Asp 45	Lys	Pro	Val
Gln	Asp 50	Arg	Gly	Leu	Val	Val 55	Thr	Asp	Ile	Lys	Ala 60	Glu	Asp	Val	Val
Leu 65	Glu	His	Arg	Ser	Tyr 70	Суѕ	Ser	Ala	Arg	Ala 75	Arg	Glu	Arg	Asn	Phe 80
Ala	Gly	Glu	Val	Leu 85	Gly	Tyr	Val	Thr	Pro 90	Trp	Asn	Ser	His	Gly 95	Tyr
Asp	Val	Ala	Lys 100		Phe	Gly	Ser	Lys 105		Thr	Gln		Ser 110	Pro	Val
Trp	Leu	Gln 115		Lys	Arg	Arg	Gly 120		Glu	Met	Phe			Thr	Gly
Leu	His 130		Val	Asp	Gln	Gly 135		Met	Arg	Ala	Val 140		Lys	His	Ala
Lys 145		Val	Arg	Ile	Val 150		Arg	Leu	Leu	Phe 155		Asp	Trp	Thr	Tyr 160
	Asp	Phe	Arg	Ser 165		Leu	Asp	Ser	Glu 170		Glu	Ile	Glu	Glu 175	
Ser	Lys	Thr	Val 180		Gln	Val	Ala	Lys 185		Gln	His	Phe	Asp 190	Gly	Phe



Val Val Glu Val Trp Ser Gln Leu Leu Ser Gln Lys His Val Gly Leu 195 200 Ile His Met Leu Thr His Leu Ala Glu Ala Leu His Gln Ala Arg Leu 210 215 220 Leu Val Ile Leu Val Ile Pro Pro Ala Val Thr Pro Gly Thr Asp Gln 225 230 235 Leu Gly Met Phe Thr His Lys Glu Phe Glu Gln Leu Ala Pro Ile Leu 245 250 255 Asp Gly Phe Ser Leu Met Thr Tyr Asp Tyr Ser Thr Ser Gln Gln Pro 260 265 270 Gly Pro Asn Ala Pro Leu Ser Trp Ile Arg Ala Cys Val Gln Val Leu 275 280 285 Asp Pro Lys Ser Gln Trp Arg Ser Lys Ile Leu Leu Gly Leu Asn Phe 295 300 Tyr Gly Met Asp Tyr Ala Ala Ser Lys Asp Ala Arg Glu Pro Val Ile 310 315 Gly Ala Arg Ala Val Leu Lys Val Ala Leu Pro Leu Ala Val Ser Ser 325 330 335 Gln Gln Ile Trp Thr Leu Gly Arg Gly Gly Ser Thr Ser Ala Leu Leu 340 345 350 Leu Ala Gly Leu Gly Leu Ala Ser Glu Pro Cys Thr Lys Ser Glu Glu 355 360 365 Val Pro Lys Lys Ser Leu Leu Asp Thr Val Trp His Trp Gln Gly Glu 370 380 375 Pro Gly Ala Leu Cys Arg Gly Arg Leu His Thr Trp Ile Leu Val Ser 390 395 Ala Val Pro Gln Ala Cys Thr Cys Leu Phe Gln 405

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Ser	Pro	Phe	Asp 180	Thr	Gln	Lys	Ile	Val 185	Ser	G1y	Gly	His	Thr 190	Val	qaA
Leu	Pro	Tyr 195	Glu	Phe	Leu	Leu	Pro 200	Cys	Met	Суз	Ile	Glu 205	Ala	Ser	Tyr
Leu	Gln 210	Glu	Asp	Thr	Val	Arg 215	Arg	Lys	Lys	Cys	Pro 220	Phe	Gln	Ser	Trp
Pro 225	`Glu	Ala	Tyr	Gly	Ser 230	Asp	Phe	Trp	Gln	Ser 235	Ile	Arg	Phe	Thr	Asp 240
Tyr	Ser	Gln	His	Asn 245	Gln	Met	Val	Met	Ala 250	Leu	Thr	Leu	Arg	Cys 255	Pro
	Lys		260					265	_		_		270		
Cys	Glu	Thr 275	Leu	Pro	Asn	Ala	Thr 280	Ala	Gln	Glu	Ser	Glu 285	Gly	Trp	Tyr
	Leu 290					295					300		_		
305	Glu	,			310					315					320
	Ser	_		325			_		330					335	
	Phe		340					345					350		-
	Gly	355					360					365			
	Thr 370	_				375					380				
385	Arg				390					395		Asp			400
	Trp			405					410			-		415	
	Leu		420			•		425	_			•	430		
	His	435	•			*	440					445			
	Glu 450					455					460				
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	Trp			485					490					495	
	Ala	_	500	_				505			_		510		
	Leu	515					520					525			
	530 Leu					535					540	_			
545	Leu				550					555	_	_			560
Ser	His	_		565					570					575	
	Leu		580					585			_		590		
		595	Cys				600		-105			605	2-3		
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Leu Tyr Arg Leu Asp Met Ser Asn Asn Leu Ser Asn Leu Pro Gln
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Gly Ile Phe Asp Asp Leu Asp Asn Ile Thr Gln Leu Ile Leu Arg Asn
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   290
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Asn Pro Trp Tyr Cys Gly Cys Lys Met Lys Trp Val Arg Asp Trp Leu
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                                  315
Gln Ser Leu Pro Val Lys Val Asn Val Arg Gly Leu Met Cys Gln Ala
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                               330
Pro Glu Lys Val Arg Gly Met Ala Ile Lys Asp Leu Ser Ala Glu Leu
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Phe Asp Cys Lys Asp Ser Gly Ile Val Ser Thr Ile Gln Ile Thr Thr 355 360 365
                        360
      355
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Ala Ile Pro Asn Thr Ala Tyr Pro Ala Gln Gly Gln Trp Pro Ala Pro
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Val Thr Lys Gln Pro Asp Ile Lys Asn Pro Lys Leu Ile Lys Asp Gln 385 390 395 400
Arg Thr Thr Gly Ser Pro Ser Arg Lys Thr Ile Leu Ile Thr Val Lys
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Ser Val Thr Pro Asp Thr Ile His Ile Ser Trp Arg Leu Ala Leu Pro
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                         425 . 430
Met Thr Ala Leu Arg Leu Ser Trp Leu Lys Leu Gly His Ser Pro Ala
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Phe Gly Ser Ile Thr Glu Thr Ile Val Thr Gly Glu Arg Ser Glu Tyr
450 460
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Leu Val Thr Ala Leu Glu Pro Glu Ser Pro Tyr Arg Val Cys Met Val
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Pro Met Glu Thr Ser Asn Leu Tyr Leu Phe Asp Glu Thr Pro Val Cys
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                               490 .
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Ile Glu Thr Gln Thr Ala Pro Leu Arg Met Tyr Asn Pro Thr Thr
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Leu Asn Arg Glu Gln Glu Lys Glu Pro Tyr Lys Asn Pro Asn Leu Pro
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Leu Ala Ala Ile Ile Gly Gly Ala Val Ala Leu Val Ser Ile Ala Leu
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                                      540
Leu Ala Leu Val Cys Trp Tyr Val His Arg Asn Gly Ser Leu Phe Ser
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                                 555
Arg Asn Cys Ala Tyr Ser Lys Gly Arg Arg Lys Asp Asp Tyr Ala
565 570 575
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                            570
                                             575
Glu Ala Gly Thr Lys Lys Asp Asn Ser Ile Leu Glu Ile Arg Glu Thr
                         585
          580
                                             590
Ser Phe Gln Met Leu Pro Ile Ser Asn Glu Pro Ile Ser Lys Glu Glu
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                                          605
Phe Val Ile His Thr Ile Phe Pro Pro Asn Gly Met Asn Leu Tyr Lys
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Asn Asn Leu Ser Glu Ser Ser Ser Asn Arg Ser Tyr Arg Asp Ser Gly
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<212> PRT <213> Rat

<400> 307

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Tyr Ser Gln Asp Asn Glu Thr Leu Glu Val Ser Pro Pro Pro Thr Ser
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Thr Tyr Gln Asp Val Ile Leu Gly Thr Arg Lys Thr Tyr Ala Val Tyr
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Asp Leu Phe Asp Thr Ala Met Ile Asn Asn Ser Arg Asn Leu Asn Ile
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           325
Gln Leu Lys Trp Lys Arg Pro Pro Asp Asn Glu Ala Leu Pro Val Pro 340 345 350
          340
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Phe Leu His Ala Gln Arg Tyr Val Ser Gly Tyr Gly Leu Gln Lys Gly
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Glu Leu Ser Thr Leu Leu Tyr Asn Ser His Pro Tyr Arg Ala Phe Pro 370 380
Val Leu Leu Leu Asp Ala Val Pro Trp Tyr Leu Arg Leu Tyr Val His 385 390 395 400
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Thr Leu Thr Ile Thr Ser Lys Gly Lys Asp Asn Lys Pro Ser Tyr Ile
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His Tyr Gln Pro Ala Gln Asp Arg Gln Gln Pro His Leu Leu Glu Met
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Glu Arg Ala Leu Leu Lys Trp Thr Glu Tyr Thr Pro Asp Pro Asn His
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Gly Phe Tyr Val Ser Pro Ser Val Leu Ser Ala Leu Val Pro Ser Met
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Val Ala Ala Lys Pro Val Asp Trp Glu Glu Ser Pro Leu Phe Asn Thr
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Glu Pro Leu Leu Val Asn Leu Pro Thr Pro Asp Phe Ser Met Pro Tyr
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Phe Tyr Asn Leu Leu Thr Arg Thr Phe His Ile Glu Glu Pro Lys Ser
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                                         45
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Phe Leu Asn Asn Ser Ile Glu Lys Ser Gly Trp Leu Phe Ile Gln Leu
                     55
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Tyr His Ser Phe Val Ser Ser Val Phe Ser Leu Phe Met Ser Arg Thr 70 75 Ser Ile Asn Gly Leu Leu Gly Arg Gly Ser Met Phe Val Phe Ser Pro 85 90 Asp Gln Phe Gln Arg Leu Leu Lys Ile Asn Pro Asp Trp Lys Thr His 100 105 110 Arg Leu Leu Asp Leu Gly Ala Gly Asp Gly Glu Val Thr Lys Ile Met 120 115 125 Ser Pro His Phe Glu Glu Ile Tyr Ala Thr Glu Leu Ser Glu Thr Met 135 140 Ile Trp Gln Leu Gln Lys Lys Lys Tyr Arg Val Leu Gly Ile Asn Glu 145 150 150 150 160Trp Gln Asn Thr Gly Phe Gln Tyr Asp Val Ile Ser Cys Leu Asn Leu 165 170 175 Leu Asp Arg Cys Asp Gln Pro Leu Thr Leu Leu Lys Asp Ile Arg Ser . 190 180 185 Val Leu Glu Pro Thr Gln Gly Arg Val Ile Leu Ala Leu Val Leu Pro 195 200 Phe His Pro Tyr Val Glu Asn Val Gly Gly Lys Trp Glu Lys Pro Ser 215 210 220 Glu Ile Leu Glu Ile Lys Gly Gln Asn Trp Glu Glu Gln Val Asn Ser 230 235 Leu Pro Glu Val Phe Arg Lys Ala Gly Phe Val Ile Glu Ala Phe Thr 250 245 255 Arg Leu Pro Tyr Leu Cys Glu Gly Asp Met Tyr Asn Asp Tyr Tyr Val 260 265 270 Leu Asp Asp. Ala Val Phe Val Leu Arg Pro Val 280 275 <210> 309 <211> 37

<212> PRT <213> Rat

<400> 309

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Arg Ala Asp Val Leu 35

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                              25
                                                30
Thr Tyr Ala Ile Asn Val Ser Leu Met Trp Leu Ser Phe Arg Lys Val
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Gln Glu Pro Gln Gly Lys Ala Lys Arg His
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Leu Val Val Met Val Cys Tyr Phe Ile Leu Ser Ile Ile Asn Ser
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Glu Lys Thr Lys
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Ala Asn Ser Arg Ser Ser Glu Asp Thr Lys Gln Met Met Ser Ser Phe
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Pro Met Thr Pro Pro Trp
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Glu Asp Thr Glu Phe

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40

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70

Gly Ala Gln Gly Met Trp Gly Ile Trp Gly His Thr Ile Thr Cys Gly

Leu Ala Pro Gly Ala Lys Pro Cys Ser Leu Lys Arg Glu Gly Pro Asp

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Leu Leu Ser Phe Pro Pro

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<210> 324 <211> 166 <212> PRT <213> Rat



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PCT/NZ01/00099

Glu Ala Pro Val Cys Gly Val Thr Glu Glu Lys Pro Glu Val Pro Asp 285 | 280 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 285 | 28

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Pro Gln Lys Glu Phe Ser Ile Pro Arg Ala His Ala Trp Pro Ser Pro 325 330 Tyr Lys Asp Tyr Glu Val Lys Lys Glu Gly Ser 340

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Gly Ser Leu Thr Gly Gly Ile Leu Ser Thr His Ser Pro 135

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Cys Gly Pro His Ala Pro Asn Lys Arg Ile Thr Asp Cys Tyr Arg Trp
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Ser Ser Phe Ser Arg Thr Val Val Ala Pro Ser Ala Val Ala Gly Lys
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Asp Gln Gly Asp Thr Thr Arg Leu Val Cys Tyr Asn Asn Lys Ile Thr

Ala Ser Tyr Glu Asp Arg Val Thr Phe Leu Pro Thr Gly Ile Thr Phe

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Pro Thr Gly Val Pro Cys Asp Pro Ile Ser Gly Leu Cys Leu Cys Pro 215 220 Pro Gly Arg Ala Gly Thr Thr Cys Asp Leu Asp Cys Arg Arg Gly Arg 225 230 235 Phe Gly Pro Gly Cys Ala Leu Arg Cys Asp Cys Gly Gly Gly Ala Asp 245 245 250 Cys Asp Pro Ile Ser Gly GIn Cys His Cys Val Asp Ser Tyr Thr Gly 260 265 Pro Thr Cys Arg Glu Val Pro Thr Gln Leu Ser Ser Ile Arg Pro Ala 275 280 Pro Gln His Ser Ser Ser Lys Ala Met Lys His 295 <210> 333 <211> 109 <212> PRT <213> Mouse <400> 333 Gly Thr Arg Val Gly Thr Pro Tyr Tyr Met Ser Pro Glu Arg Ile His 10 Glu Asn Gly Tyr Asn Phe Lys Ser Asp Ile Trp Ser Leu Gly Cys Leu . 20 25 Leu Tyr Glu Met Ala Ala Leu Gln Ser Pro Phe Tyr Gly Asp Lys Met 35 40 45 Asn Leu Tyr Ser Leu Cys Lys Lys Ile Glu Gln Cys Asp Tyr Pro Pro 60 55 Leu Pro Ser Asp His Tyr Ser Glu Glu Leu Arg Gln Leu Val Asn Ile

Cys Ile Asn Pro Asp Pro Glu Lys Arg Pro Asp Ile Ala Tyr Val Tyr

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75

90



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Leu 145	Lys	Pro	Ala	Asn	Ile 150	Leu	Leu	Asp	Ala	His 155	Tyr	His	Val	ГЛЗ	Ile 160
Ser	Asp	Phe	Gly	Leu 165	Ala	Lys	Cys	Asn	Gly 170	Met	Ser	His	Ser	His 175	Asp
Leu	Ser	Met	Asp 180	Gly	Leu	Phe	Gly	Thr 185	Ile	Ala	Tyr	Leu	Pro 190	Pro	Glu
Arg	Ile	Arg 195	Glu	Lys	Ser	Arg	Leu 200	Phe	Asp	Thr	Lys	His 205	Asp	Val	Tyr
Ser	Phe 210	Ala	Ile	Val	Ile	Trp 215	Gly	Val	Leu	Thr	Gln 220	Lys	Lys	Pro	Phe
Ala 225	Asp	Glu	Lys	Asn	Ile 230	Leu	His	Ile _.	Met	Met 235	Lys	Val	Val	Lys	G1y 240
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305	Ser				310					315					320
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Gly	Asp			405					410					415	
Ile			Gly 420					425					430		
	Val	435					440					445			
	Glu 450		_			455					460				
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Lys			Val 500					505					510		
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545	Val				550					555					560
	Arg			565					570					575	
Leu	His	Tyr	Ala	Ala	Trp	Gln	Gly	His	Leu	Pro	Ile	Val	Lys	Leu	Leu



585 Ala Lys Gln Pro Gly Val Ser Val Asn Ala Gln Thr Leu Asp Gly Arg 595 600 605 Thr Pro Leu His Leu Ala Ala Gln Arg Gly His Tyr Arg Val Ala Arg 615 620 Ile Leu Ile Asp Leu Cys Ser Asp Val Asn Ile Cys Ser Leu Gln Ala 625 630 635 640 625 630 635 Gln Thr Pro Leu His Val Alà Ala Glu Thr Gly His Thr Ser Thr Ala 645 650 Arg Leu Leu His Arg Gly Ala Gly Lys Glu Ala Leu Thr Ser Glu 660 665 670 Gly Tyr Thr Ala Leu His Leu Ala Ala Gln Asn Gly His Leu Ala Thr 675 680 685 Val Lys Leu Leu Ile Glu Glu Lys Ala Asp Val Met Ala Arg Gly Pro 695 700 Leu Asn Gln Thr Ala Leu His Leu Ala Ala Ala Arg Gly His Ser Glu 710 715 Gln Gly Leu Ser Ala Leu His Leu Ala Ala Gln Gly Arg His Ser Gln 740 · 745 750 Thr Val Glu Thr Leu Leu Lys His Gly Ala His Ile Asn Leu Gln Ser 755 760 Leu Lys Phe Gln Gly Gly Gln Ser Ser Ala Ala Thr Leu Leu Arg Arg 770 775 780 Ser Lys Thr 785 <210> 335 <211> 194 <212> PRT <213> Mouse

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195 200 205 Ile Arg Ala Gly Asn Ser Gln Gly Asp Phe Tyr Ile Arg Gln Ile Asn 210 215 220 Asn Val Ser Ala Met Leu Val Leu Ala Arg Pro Val Thr Gly Pro Arg 230 235 Glu Tyr Val Leu Asp Leu Glu Met Val Thr Met Asn Ser Leu Met Ser 245 250 Tyr Arg Ala Ser Ser Val Leu Arg Leu Thr Val Phe Val Gly Ala Tyr 260 265 270 Thr Phe

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165 170 175 Leu Glu Gly Asn Ser Cys Glu Ile Phe Trp Glu Thr Val Pro Pro Met Arg Gly Asp Pro Val Ser Tyr Val Leu Gln Val Leu Val Gly Arg Asp Ser Glu Tyr Lys Gln Val Tyr Lys Gly Glu Glu Ala Thr Phe Gln Ile 210 215 220 Ser Gly Leu Gln Ser Asn Thr Asp Tyr Arg Phe Arg Val Cys Ala Cys . 230 Arg Arg Cys Val Asp Thr Ser Gln Glu Leu Ser Gly Ala Phe Ser Pro Ser Ala Ala Phe Met Leu Gln Gln Arg Glu Val Met Leu Thr Gly Asp Leu Gly Gly Met Glu Glu Ala Lys Met Lys Gly Met Met Pro Thr Asp 275 280 285 Glu Gln Phe Ala Ala Leu Ile Val Leu Gly Phe Ala Thr Leu Ser Ile Leu Phe Ala Phe Ile Leu Gln Tyr Phe Leu Met Lys

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Gln Thr Asn Trp Thr Val Pro Thr Ser Glu Asp Val Thr Lys Val Asn 115 120 125 Leu Gln Val Leu Ile Val Val Asn Arg Thr Ala Ser Lys Ser Ser Val 130 135 140 Lys Met Glu Gln Val Gln Pro Ser Ala Ser Thr Pro Ile Pro Glu Ser 150 155 145 Ser Glu Thr Ser Gln Thr Ile Asn Thr Thr Pro Thr Val Asn Thr Ala 1.65 170 1.75 Lys Thr Thr Ala Lys Asp Thr Ala Asn Thr Thr Ala Val Thr Thr Ala 180 185 190 Asn Thr Thr Ala Asn Thr Thr Ala Val Thr Thr Ala Lys Thr Thr Ala 195 200 205 Lys Ser Leu Ala Ile Arg Thr Leu Gly Ser Pro Leu Ala Gly Ala Leu 215 210 220 His Ile Leu Leu Val Phe Leu Ile Ser Lys Leu Leu Phe

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265



Ser Asp Gln Glu Thr Leu Arg Ile His Glu Arg Leu Val Ala Gly Ser 275 280 285 Leu Ala Gly Ala Ile Ala Gln Ser Ser Ile Tyr Pro Met Glu Val Leu 290 295 300 Lys Thr Arg Met Ala Leu Arg Lys Thr Gly Gln Tyr Ser Gly Met Leu 305 310 315 320 Asp Cys Ala Arg Arg Ile Leu Ala Lys Glu Gly Val Ala Ala Phe Tyr 325 330 Lys Gly Tyr Ile Pro Asn Met Leu Gly Ile Ile Pro Tyr Ala Gly Ile 340 345 350 Asp Leu Ala Val Tyr Glu Thr Leu Lys Asn Thr Trp Leu Gln Arg Tyr 355 360 365 355 360 365 Ala Val Asn Ser Ala Asp Pro Gly Val Phe Val Leu Leu Ala Cys Gly 375 380 Thr Ile Ser Ser Thr Cys Gly Gln Leu Ala Ser Tyr Pro Leu Ala Leu 385 390 395 Val Arg Thr Arg Met Gln Ala Gln Ala Ser Ile Glu Gly Ala Pro Glu 415 Val Thr Met Ser Ser Leu Phe Lys Gln Ile Leu Arg Thr Glu Gly Ala 420 425 Phe Gly Leu Tyr Arg Gly Leu Ala Pro Asn Phe Met Lys Val Ile Pro 435 440 445 Ala Val Ser Ile Şer Tyr Val Val Tyr Glu Asn Leu Lys Ile Thr Leu 450 455 460 Gly Val Gln Ser Arg 465

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165 170

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Ala Val Asp Ile Leu Phe Leu Leu Asp Gly Ser His Ser Ile Gly Lys
 50 55
                            60
Gly Ser Phe Glu Arg Ser Lys Arg Phe Ala Ile Ala Ala Cys Asp Ala
65 70 75 80
Leu Asp Ile Ser Pro Gly Arg Val Arg Val Gly Ala Leu Gln Phe Gly 85 90
Ser Thr Pro His Leu Glu Phe Pro Leu Asp Ser Phe Ser Thr Arg Gln
      100 105
Glu Val Lys Glu Ser Ile Lys Gly Ile Val Phe Lys Gly Gly Arg Thr 115 120 125
Glu Thr Gly Leu Ala Leu Lys Arg Leu Ser Arg Gly Phe Pro Gly Gly
  130 135 140
Arg Asn Gly Ser Val Pro Gln Ile Leu Ile Ile Val Thr Asp Gly Lys 145 150 155 160
Ser Gln Gly Pro Val Ala Leu Pro Ala Lys Gln Leu Arg Glu Arg Gly
165 170 175
Gln Val Glu Asp Ala Thr Asn Gly Leu Leu Ser Thr Leu Ser Ser Ser
 210 215 220
Ala Leu Cys Thr Thr Ala Asp Pro Asp Cys Arg Val Glu Pro His Pro 225 230 235 240
Cys Glu Arg Arg Thr Leu Glu Thr Val Arg Glu Leu Ala Gly Asn Ala
            245 250
                                              255
Leu Cys Trp Arg Gly Ser Arg Gln Ala Asp Thr Val Leu Ala Leu Pro
        260 265 270
Cys Pro Phe Tyr Ser Trp Lys Arg Val Phe Gln Thr His Pro Ala Asn 275 280 285
Cys Tyr Arg Thr Ile Cys Pro Gly Pro Cys Asp Ser Gln Pro Cys Gln
290 295 300
                           300
Asn Gly Gly Thr Cys Ile Pro Glu Gly Val Asp Arg Tyr His Cys Leu
              310
                             315
Cys Pro Leu Ala Phe Gly Gly Glu Val Asn Cys Ala Pro Lys Leu Ser
325 330 335
Leu Glu Cys Arg Ile Asp Val Leu Phe Leu Leu Asp Ser Ser Ala Gly 340 350
Thr Thr Leu Gly Gly Phe Arg Arg Ala Lys Ala Phe Val Lys Arg Phe
```

```
355
                        360
Val Gln Ala Val Leu Arg Glu Asp Ser Arg Ala Arg Val Gly Ile Ala 370 380
Ser Tyr Gly Arg Asn Leu Met Val Ala Val Pro Cys Arg Gly Val Pro
385 390
                         395
Ala Leu Cys Arg Thr
    <210> 375
     <211> 180
     <212> PRT
     <213> Mouse
     <400> 375
Met Glu Leu Ser Asp Val Thr Leu Ile Glu Gly Val Gly Asn Glu Val 1 5 10 15
Met Val Val Ala Gly Val Val Ala Leu Thr Leu Ala Leu Val Leu Ala
       20
                  25 30
Trp Leu Ser Thr Tyr Val Ala Asp Ser Gly Asn Asn Gln Leu Leu Gly
  35
                     40
                                         45
Thr Ile Val Ser Ala Gly Asp Thr Ser Val Leu His Leu Gly His Val 50 60
Asp Gln Leu Val Asn Gln Gly Thr Pro Glu Pro Thr Glu His Pro His
65 . 70 . 75 . 80
Pro Ser Gly Gly Asn Asp Asp Lys Ala Glu Glu Thr Ser Asp Ser Gly
             85
                             90
Gly Asp Ala Thr Gly Glu Pro Gly Ala Arg Gly Glu Met Glu Pro Ser
Leu Glu His Leu Leu Asp Ile Gln Gly Leu Pro Lys Arg Gln Ala Gly 115 · 120 125
Leu Gly Ser Ser Arg Pro Glu Ala Pro Leu Gly Leu Asp Asp Gly Ser
 130 135 140
Cys Leu Ser Pro Ser Pro Ser Leu Ile Asn Val Arg Leu Lys Phe Leu
145 150 160
Asn Asp Thr Glu Glu Leu Ala Val Ala Arg Pro Glu Asp Thr Val Gly
 165
                      170
Thr Leu Lys Arg
. 180
    <210> 376
    <211> 68
    <212> PRT
    <213> Mouse
    <400> 376
Met Cys Leu Pro Val Thr Val Trp Cys His Trp Ala Leu Trp Val Aļa
1 5 10 . 15
His Leu Pro Leu Ile Pro Ser Val Gly Lys Ser Gln Cys Thr Gln Met
 20 25 30
Trp His Cys Cys Met Pro Trp Val Cys Val Gly Asp Cys Leu Cys Leu 35 40 45
Ser Asp Pro Leu Trp Leu Cys Leu Leu Lys Glu Thr Glu Thr Pro Cys
 50
               55
Gly Phe Leu Ser
    <210> 377
```

```
<211> 107
      <212> PRT
      <213> Rat
     <400> 377
Met Pro Phe Arg Leu Leu Ile Pro Leu Gly Leu Val Cys Val Leu Leu
               5
                                 10
Pro Leu His His Gly Ala Pro Gly Pro Glu Gly Thr Ala Pro Asp Pro
                                            30
Ala His Tyr Arg Glu Arg Val Lys Ala Met Phe Tyr His Ala Tyr Asp 35 40 45
Ser Tyr Leu Glu Asn Ala Phe Pro Tyr Asp Glu Leu Arg Pro Leu Thr 50 60
Cys Asp Gly His Asp Thr Trp Gly Ser Phe Ser Leu Thr Leu Ile Asp 65 70 75 80
Ala Leu Asp Thr Leu Leu Ile Leu Gly Asn Thr Ser Glu Phe Gln Arg 85 90 95
Val Val Glu Val Leu Gln Asp Lys Arg Gly Leu
          100
                   105
      <210> 378
      <211> 95
      <212> PRT
      <213> Rat
     <400> 378
Ser Gln Ala Ser Pro His Trp Pro Tyr Gly Ile Ile Ser Gly Gly Gln 20 25 30
Glu Gly Leu Cys Arg Leu Trp Thr Ala Thr Cys His Ser Arg Gly Glu
     35 40
                                         45
Ser Glu Val Ser Arg Ser Ser Arg Lys Glu Asp Pro Arg Ile Pro Gln 50 60
Gly Ser Leu Ser Gly Asn Val Asp Phe Trp Arg Val Cys Pro Pro Cys 65 70 75 80
Ala His Thr Ser Met Asp Arg Thr Leu Gly Leu Leu Ser Cys Cys
   85
                                   90
     <210> 379
     <211> 138
     <212> PRT
     <213> Mouse
     <400> 379
Met Asp Leu Asp Val Val Asn Met Phe Val Ile Ala Gly Gly Thr Leu 1 5 10 10 15 15
Ala Ile Pro Ile Leu Ala Phe Val Ala Ser Phe Leu Leu Trp Pro Ser 20 25 . 30
Ala Leu Ile Arg Ile Tyr Tyr Trp Tyr Trp Arg Arg Thr Leu Gly Met 35 \hspace{1cm} 40 \hspace{1cm} 45
Gln Val Arg Tyr Ala His His Glu Asp Tyr Gln Phe Cys Tyr Ser Phe 50 55 60
Arg Gly Arg Pro Gly His Lys Pro Ser Ile Leu Met Leu His Gly Phe 65 70 75 80
Ser Ala His Lys Asp Met Trp Leu Ser Val Val Lys Phe Leu Pro Lys
                                , 90
```

```
Asn Leu His Leu Val Cys Val Asp Met Pro Gly His Glu Gly Thr Thr
       100 105 110.
Arg Ser Ser Leu Asp Asp Leu Ser Ile Val Gly Gln Val Lys Arg Ile
    115 120
His Gln Phe Val Glu Cys Leu Lys Leu Asn
 130
                   135
     <210> 380
    <211> 81
    <212> PRT
    <213> Rat
    <400> 380
Met Ala Ser Ser Ser Asn Trp Leu Ser Gly Val Asn Val Val Leu Val
1 5 10
                          10
Met Ala Tyr Gly Ser Leu Val Phe Val Leu Leu Phe Ile Phe Val Lys
 20 25 30
Arg Gln Ile Met Arg Phe Ala Met Lys Ser Arg Arg Gly Pro His Val
      35
                     40
                                    45
Pro Val Gly His Asn Ala Pro Lys Asp Leu Lys Glu Glu Ile Asp Ile
50 55
                                   60
Arg Leu Ser Arg Val Gln Asp Ile Lys Tyr Glu Pro Gln Leu Leu Ala
65 70
                         75
    <210> 381
    <211> 257
    <212> PRT
    <213> Mouse
    <400> 381
Met Arg Ser Gly Ala Leu Trp Pro Leu Leu Trp Gly Ala Leu Val Trp 1 5 10
                           10
Thr Val Gly Ser Val Gly Ala Val Met Gly Ser Glu Asp Ser Val Pro
 20 25
                                 30
Gly Gly Val Cys Trp Leu Gln Gln Gly Arg Glu Ala Thr Cys Ser Leu
      35
                      40
                                        45
Val Leu Lys Thr Arg Val Ser Arg Glu Glu Cys Cys Ala Ser Gly Asn
 50 55
Ile Asn Thr Ala Trp Ser Asn Phe Thr His Pro Gly Asn Lys Ile Ser 65 70 75 80
                              75
Leu Leu Gly Phe Leu Gly Leu Val His Cys Leu Pro Cys Lys Asp Ser
           85
                             90
                                              95
Cys Asp Gly Val Glu Cys Gly Pro Gly Lys Ala Cys Arg Met Leu Gly
         100 105 110
Gly Arg Pro Thr Leu Arg Ser Cys Val Pro Asn Cys Glu Gly Leu Pro
115 120 125
Ala Gly Phe Gln Val Cys Gly Ser Asp Gly Ala Thr Tyr Arg Asp Glu
130 135
Cys Glu Leu Arg Thr Ala Arg Cys Arg Gly His Pro Asp Leu Arg Val
       150 155
Met Tyr Arg Gly Arg Cys Gln Lys Ser Cys Ala Gln Val Val Cys Pro
165 170 175
Arg Pro Gln Ser Cys Leu Val Asp Gln Thr Gly Ser Ala His Cys Val
180 185 190
Val Cys Arg Ala Ala Pro Cys Pro Val Pro Ser Asn Pro Gly Gln Glu
```

```
195
                         200
Leu Cys Gly Asn Asn Asn Val Thr Tyr Ile Ser Ser Cys His Leu Arg 210 215 220
Gln Ala Thr Cys Phe Leu Gly Arg Ser Ile Gly Val Arg His Pro Gly
225 230 235 240
Ile Cys Thr Gly Gly Pro Lys Val Pro Ala Glu Glu Glu Asn Phe
        245 250
     <210> 382
     <211> 285
     <212> PRT.
     <213> Rat
     <400> 382
Met Ile Ser Trp Met Leu Leu Ala Cys Ala Leu Pro Cys Ala Ala Asp
1 5
                               10 . 15
Pro Met Leu Gly Ala Phe Ala Arg Arg Asp Phe Gln Lys Gly Gly Pro 20 25 30
Gln Leu Val Cys Ser Leu Pro Gly Pro Gln Gly Pro Pro Gly Pro Pro 35 40
Gly Ala Pro Gly Ser Ser Gly Met Val Gly Arg Met Gly Phe Pro Gly
 50 55
                              60
Lys Asp Gly Gln Asp Gly Gln Asp Gly Asp Gly Asp Ser Gly Glu 65 70 75 80
Glu Gly Pro Pro Gly Arg Thr Gly Asn Arg Gly Lys Gln Gly Pro Lys
85 90 95
Gly Lys Ala Gly Ala Ile Gly Arg Ala Gly Pro Arg Gly Pro Lys Gly 100 $105$
Val Ser Gly Thr Pro Gly Lys His Gly Ile Pro Gly Lys Lys Gly Pro
115 120 125
                                          125
Lys Gly Lys Lys Gly Glu Pro Gly Leu Pro Gly Pro Cys Ser Cys Gly 130 135 140
Ser Ser Arg Ala Lys Ser Ala Phe Ser Val Ser Val Thr Lys Ser Tyr
145 150 155 160
Pro Arg Glu Arg Leu Pro Ile Lys Phe Asp Lys Ile Leu Met Asn Glu
. 165 170 175
Gly Gly His Tyr Asn Ala Ser Ser Gly Lys Phe Val Cys Ser Val Pro
180 185 190
Gly Ile Tyr Tyr Phe Thr Tyr Asp Ile Thr Leu Ala Asn Lys His Leu
195 200 205
Ala Ile Gly Leu Val His Asn Gly Gln Tyr Arg Ile Arg Thr Phe Asp
  210 215 220
Ala Asn Thr Gly Asn His Asp Val Ala Ser Gly Ser Thr Ile Leu Ala
225 230 235 240
Leu Lys Glu Gly Asp Glu Val. Trp Leu Gln Ile Phe Tyr Ser Glu Gln 245 250 255
Asn Gly Leu Phe Tyr Asp Pro Tyr Trp Thr Asp Ser Leu Phe Thr Gly 260 265 270
Phe Leu Ile Tyr Ala Asp Gln Gly Asp Pro Asn Glu Val
     275 280 285
     <210> 383
     <211> 183
     <212> PRT
     <213> Rat
```

```
<400> 383
Met Lys Leu Leu Cys Leu Val Ala Val Val Gly Cys Leu Leu Val Pro
                             10
Pro Ala Gln Ala Asn Lys Ser Ser Glu Asp Ile Arg Cys Lys Cys Ile
         20
                         2.5
                                     30
Cys Pro Pro Tyr Arg Asn Ile Ser Gly His Ile Tyr Asn Gln Asn Val
  35 ` 40
Ser Gln Lys Asp Cys Asn Cys Leu His Val Val Glu Pro Met Pro Val
50 60
Pro Gly His Asp Val Glu Ala Tyr Cys Leu Leu Cys Glu Cys Arg Tyr 65 70 75 80
Glu Glu Arg Ser Thr Thr Thr Ile Lys Val Ile Ile Val Ile Tyr Leu
85 90
Ser Val Val Gly Ala Leu Leu Leu Tyr Met Ala Phe Leu Met Leu Val
Asp Pro Leu Ile Arg Lys Pro Asp Ala Tyr Thr Glu Gln Leu His Asn
  115 120 125
Glu Glu Glu Asn Glu Asp Ala Arg Ser Met Ala Ala Ala Ala Ala Ser
 130 135 140
Ile Gly Gly Pro Arg Ala Asn Thr Val Leu Glu Arg Val Glu Gly Ala 145 150 155 160
Gln Gln Arg Trp Lys Leu Gln Val Gln Glu Gln Arg Lys Thr Val Phe
          165 170 175
Asp Arg His Lys Met Leu Ser
      180
     <210> 384
     <211> 292
     <212> PRT
     <213> Mouse
     <400> 384
Cys Gln Leu Pro Leu Arg Val Leu Ile Ile Ser Asn Asn Lys Leu Gly
1 5 10 15
Ala Leu Pro Pro Asp Ile Ser Thr Leu Gly Ser Leu Arg Gln Leu Asp
       20
                         25
Val Ser Ser Asn Glu Leu Gln Ser Leu Pro Val Glu Leu Cys Ser Leu
    35 40 45
Arg Ser Leu Arg Asp Leu Asn Val Arg Arg Asn Gln Leu Ser Thr Leu 50^{\circ} 60^{\circ}
Pro Asp Glu Leu Gly Asp Leu Pro Leu Val Arg Leu Asp Phe Ser Cys
                70
                              75
Asn Arg Ile Ser Arg Ile Pro Val Ser Phe Cys Arg Leu Arg His Leu
           85 90
Gln Val Val Leu Leu Asp Ser Asn Pro Leu Gln Ser Pro Pro Ala Gln
100 105 110
Ile Cys Leu Lys Gly Lys Leu His Ile Phe Lys Tyr Leu Thr Met Glu
    115 120
Ala Gly Arg Arg Gly Ala Ala Leu Gly Asp Leu Val Pro Ser Arg Pro 130 140
Pro Ser Phe Ser Pro Cys Pro Ala Glu Asp Leu Phe Pro Gly Arg Arg 145
Tyr Asp Gly Gly Leu Asp Ser Gly Phe His Ser Val Asp Ser Gly Ser
            165 170 175
Lys Arg Trp Ser Gly Asn Glu Ser Thr Asp Asp Phe Ser Glu Leu Ser
         180
                          185
                                      190
```

```
Phe Arg Ile Ser Glu Leu Ala Arg Asp Pro Arg Gly Pro Arg Gln Pro 195 200 205
Arg Glu Asp Gly Ala Gly Asp Gly Asp Leu Glu Gln Ile Asp Phe Ile
210 215 220
Asp Ser His Val Pro Gly Glu Asp Glu Asp Arg Ser Ala Ala Glu Glu
225 230 235 240
Gln Leu Pro Ser Glu Leu Ser Leu Val Ala Gly Asp Val Glu Lys Pro
245 250 255
Ser Ser Ser Arg Arg Glu Glu Pro Ala Gly Glu Glu Arg Arg Pro
260 265 270
Asp Thr Leu Gln Leu Trp Gln Glu Arg Glu Arg Lys Gln Gln Gln Gln
    275 280
Ser Gly Gly Trp
   290
    <210> 385
    <211> 164
     <212> PRT
     <213> Mouse
    <400> 385
Ser Arg Gln Leu Arg Ala Pro Arg Phe Asp Pro Arg Ala Gly Phe His 1 \phantom{0} 5 \phantom{0} 10 \phantom{0} 10 \phantom{0} 15
Ala Glu Gly Lys Asp Arg Gly Pro Ser Val Pro Gln Gly Leu Leu Lys
      20
                        25 30
Ala Ala Arg Ser Ser Gly Gln Leu Asn Leu Ala Gly Arg Asn Leu Gly 35
Ala Asn Gln Asn Leu Ser Phe Ser Ser Thr Glu Arg Trp Trp Asp Gln
65 70 75
Thr Asp Leu Thr Lys Leu Ile Ile Ser Ser Asn Lys Leu Gln Ser Leu
85 90 95
Ser Asp Asp Leu Arg Leu Leu Pro Ala Leu Thr Val Leu Asp Ile His
Asp Asn Gln Leu Thr Ser Leu Pro Ser Ala Ile Arg Glu Leu Asp Asn
  115 120 125
Leu Gln Lys Leu Asn Val Ser His Asn Lys Leu Lys Ile Leu Pro Glu
130 135 140
Glu Ile Thr Ser Leu Lys Asn Leu Arg Thr Leu His Leu Gln His Asn
145
       150
                         155
Glu Leu Thr Cys
    <210> 386
    <211> 71'
     <212> PRT
    <213> Mouse
    <400> 386
Ser Leu Ser Ile Leu Pro Ala Val Arg Val Ser Pro Arg Pro Thr Tyr 1 5 10 15
Pro Ser Thr Ala Ser Ser Met Ala Ala Phe Leu Val Thr Gly Phe Phe
  20 25 30
Phe Ser Leu Phe Val Val Leu Gly Met Glu Pro Arg Ala Leu Phe Arg
    35 40 45
Pro Asp Lys Ala Leu Pro Leu Ser Cys Ala Lys Pro Thr Ser Leu Cys
```

```
50
                                         60
Val Gln Ser Ser Phe Leu Gly
     <210> 387
     <211> 126
     <212> PRT
     <213> Mouse
     <400> 387
Glu Tyr Glu Ala Arg Val Leu Glu Lys Ser Leu Arg Lys Glu Ser Arg
1 5 10
Asn Lys Glu Thr Asp Lys Val Lys Leu Thr Trp Arg Asp Arg Phe Pro
                            25
  20
                                          30
Ala Tyr Phe Thr Asn Leu Val Ser Ile Ile Phe Met Ile Ala Val Thr 35 40 45
Phe Ala Ile Val Leu Gly Val Ile Ile Tyr Arg Ile Ser Thr Ala Ala 50 55 60
Ala Leu Ala Met Asn Ser Ser Pro Ser Val Arg Ser Asn Ile Arg Val
                  70
                                  75
Thr Val Thr Ala Thr Ala Val Ile Ile Asn Leu Val Val Ile Ile Leu 85 90 95
Leu Asp Glu Val Tyr Gly Cys Ile Ala Arg Trp Leu Thr Lys Ile Gly
100 105 110
Glu Cys His Val Gln Asp Ser Ile Gly Ser Met Gly Leu Gly
      115 120
     <210> 388
     <211> 84
     <212> PRT
     <213> Rat
     <400> 388
Ala Ala Glu Asn Glu Met Pro Val Ala Val Gly Pro Tyr Gly Gln Ser 1 5 10 15
Gln Pro Ser Cys Phe Asp Arg Val Lys Met Gly Phe Val Met Gly Cys 20 25 30
Ala Val Gly Met Ala Ala Gly Ala Leu Phe Gly Thr Phe Ser Cys Leu
    35
                         40
                                         45
Arg Ile Gly Met Arg Gly Arg Glu Leu Met Gly Gly Ile Gly Lys Thr
 50 55 60
Met Met Gln Ser Gly Gly Thr Phe Gly Thr Phe Met Ala Ile Gly Met
                 70
                                     75
Gly Ile Arg Cys
     <210> 389
     <211> 284
     <212> PRT
     <213> Rat
     <400> 389
Gly Gly Ser Ser Val Ser His Val Leu Arg Gly Ser Gly Gln Glu Arg
1 5 10 15
Ser Pro Pro Pro Ala Ser Met Gln Pro Pro Trp Gly Leu Ala Leu Pro 20 25 30
Leu Leu Pro Trp Val Ala Gly Gly Val Gly Thr Ser Pro Arg Asp
```

```
40
Tyr Trp Leu Pro Ala Leu Ala His Gln Pro Gly Val Cys His Tyr Gly 50 60
Thr Lys Thr Ala Cys Cys Tyr Gly Trp Lys Arg Asn Ser Lys Gly Val 65 70 75 80
Cys Glu Ala Val Cys Glu Pro Arg Cys Lys Phe Gly Glu Cys Val Gly
85 90
Pro Asn Lys Cys Arg Cys Phè Pro Gly Tyr Thr Gly Lys Thr Cys Ser
100 105 110
Gln Asp Val Asn Glu Cys Ala Phe Lys Pro Arg Pro Cys Gln His Arg
115 120 125
Cys Val Asn Thr His Gly Ser Tyr Lys Cys Phe Cys Leu Ser Gly His
130 140
Met Leu Leu Pro Asp Ala Thr Cys Ser Asn Ser Arg Thr Cys Ala Arg 145 150 155 160
Ile Asn Cys Gln Tyr Ser Cys Glu Asp Thr Ala Glu Gly Pro Arg Cys
165 170 175
Val Cys Pro Ser Ser Gly Leu Arg Leu Gly Pro Asn Gly Arg Val Cys
180 185 190
Leu Asp Ile Asp Glu Cys Ala Ser Ser Lys Ala Val Cys Pro Ser Asn 195 200 205
Arg Arg Cys Val Asn Thr Phe Gly Ser Tyr Tyr Cys Lys Cys His Ile 210 225
Gly Phe Glu Leu Lys Tyr Ile Ser Arg Arg Tyr Asp Cys Val Asp Ile
225 230 235 240
Asn Glu Cys Thr Leu Asn Thr Arg Thr Cys Ser Pro His Ala Asn Cys
          245 250 255
Leu Asn Thr Gln Gly Ser Phe Lys Cys Lys Cys Lys Gln Gly Tyr Arg 260 265 270
Gly Asn Gly Leu Gln Cys Ser Val Ile Pro Glu His
       275
                  280
      <210> 390
      <211> 85
      <212> PRT
      <213> Rat
     <400> 390
Gly Ala Pro Met Tyr Phe Ser Glu Gly Arg Glu Arg Gly Lys Val Tyr
1 5 10
Val Tyr Asn Leu Arg Gln Asn Arg Phe Val Phe Asn Gly Thr Leu Lys 20 25 30
Asp Ser His Ser Tyr Gln Asn Ala Arg Phe Gly Ser Cys Ile Ala Ser 35 40 45
Val Gln Asp Leu Asn Gln Asp Ser Tyr Asn Asp Val Val Val Gly Ala
 50 55
                                    60
Pro Gln Glu Asp Ser His Arg Gly Ala Ile Tyr Ile Phe His Gly Phe 65 75 80
Gln Thr Asn Ile Leu
     <210> 391
     <211> 158
      <212> PRT
      <213> Rat
      <400> 391
```

```
Phe Gln Thr Asn Ile Leu Lys Lys Pro Val Gln Arg Ile Ser Ala Ser 1 5 10
Glu Leu Ala Pro Gly Leu Gln His Phe Gly Cys Ser Ile His Gly Gln
          20
Leu Asp Leu Asn Glu Asp Gly Leu Val Asp Leu Ala Val Gly Ala Leu
  35
                        40
Gly Asn Ala Val Val Leu Trp Ala Arg Pro Val Val Gln Ile Asn Ala 50 55
Ser Leu His Phe Glu Pro Ser Lys Ile Asn Ile Phe His Lys Asp Cys 65 70 75 80
Lys Arg Asn Gly Arg Asp Ala Thr Cys Leu Ala Ala Phe Leu Cys Phe 85 90 95
Gly Pro Ile Phe Leu Ala Pro His Phe His Thr Ala Thr Val Gly Ile
100 105 110
Arg Tyr Asn Ala Thr Met Asp Glu Arg Arg Tyr Met Pro Arg Ala His
115 120 125
Leu Asp Glu Gly Ala Asp Gln Phe Thr Asn Arg Ala Val Leu Leu Ser
 130 135 140
Ser Gly Gln Glu His Cys Gln Arg Ile Asn Phe His Val Leu
                   150
                              155
     <210> 392
     <211> 124
     <212> PRT
      <213> Mouse
     <400> 392
Ala Ala Glu Gln Glu Ala Ser Ser Arg Arg Arg Gly Gly Ala Gly
                                   10
Pro Ala Leu Phe Ser Ser Gly Ser Leu Arg Ser Glu Pro Gln Pro Arg 20 25 30
Leu Pro Gln Ala Arg Ser Arg Pro Arg Pro Ser Phe Leu Gln Ala Arg 35 40 45
Ser Arg Pro Cys Leu Ser Gln Ala Cys Ser Pro Ala Ala Ser Val Leu 50 60
Ser Ser Ser Ser Leu Cys Gly Arg Ser His Leu Leu Pro Gly Ser Leu 65 70 75 80
Pro Ala Thr Ala Phe Leu Leu Leu Pro Gly Ser Leu Pro Gly Arg 85 90 95
                                90 95
Arg Pro Ser Ala Ala Gln Ala Ala Pro Val Leu Ala Trp Gly Leu Val
100 105 110
                                                  110
Ala Phe Gln Leu Gly Val Ala Ala Gly Ala Gly Arg
                           120
     <210> 393
      <211> 242
      <212> PRT
     <213> Rat
      <400> 393
Gly His Cys Asp Cys Gln Ala Gly Tyr Gly Glu Ala Cys Gly Gln 1 5 15
Cys Gly Leu Gly Tyr Phe Glu Ala Glu Arg Asn Ser Ser His Leu Val 20 25 30
Cys Ser Ala Cys Phe Gly Pro Cys Ala Arg Cys Thr Gly Pro Glu Glu 35 40 45
Ser His Cys Leu Gln Cys Arg Lys Gly Trp Ala Leu His His Leu Lys
```

```
55
Cys Val Asp Ile Asp Glu Cys Gly Thr Glu Gln Ala Thr Cys Gly Ala 65 70 75 80
Asp Gln Phe Cys Val Asn Thr Glu Gly Ser Tyr Glu Cys Arg Asp Cys
              85
                                     90
Ala Lys Ala Cys Leu Gly Cys Met Gly Ala Gly Pro Gly Pro Cys Lys
Lys Cys Ser Arg Gly Tyr Gln Gln Val Gly Ser Lys Cys Leu Asp Val 115 120 125
Asp Glu Cys Glu Thr Val Val Cys Pro Gly Glu Asn Glu Gln Cys Glu
130 135 140
Asn Thr Glu Gly Ser Tyr Arg Cys Val Cys Ala Glu Gly Phe Arg Gln 145 155 160
Glu Asp Gly Ile Cys Val Lys Glu Gln Ile Pro Glu Ser Ala Gly Phe
165 170 175
Phe Ala Glu Met Thr Glu Asp Glu Met Val Val Leu Gln Gln Met Phe
            180 185 190
Phe Gly Val Ile Ile Cys Ala Leu Ala Thr Leu Ala Ala Lys Gly Asp
195 200 205
Leu Val Phe Thr Ala Ile Phe Ile Gly Ala Val Ala Ala Met Thr Gly
210 220
Tyr Trp Leu Ser Glu Arg Ser Asp Arg Val Leu Glu Gly Phe Ile Lys 235 240
Gly Arg
```

<210> 394

<211> 99

<212> PRT

<213> Mouse

<400> 394

Met Arg Leu Leu Ala Ala Ala Leu Leu Leu Leu Leu Ala Leu Cys . 1 5 10 15 Ala Ser Arg Val Asp Gly Ser Lys Cys Lys Cys Ser Arg Lys Gly Pro
20 25 30 Lys Ile Arg Tyr Ser Asp Val Lys Lys Leu Glu Met Lys Pro Lys Tyr . 35 40 45 Pro His Cys Glu Glu Lys Met Val Ile Val Thr Thr Lys Ser Met Ser 50 60 Arg Tyr Arg Gly Gln Glu His Cys Leu His Pro Lys Leu Gln Ser Thr 70 75 80 Lys Arg Phe Ile Lys Trp Tyr Asn Ala Trp Asn Glu Lys Arg Arg Val 90 Tyr Glu Glu

<210> 395 <211> 103

<212> PRT

<213> Human

<400> 395

Met Ala Leu Gly Val Pro Ile Ser Val Tyr Leu Leu Phe Asn Ala Met 5 10 15 Thr Ala Leu Thr Glu Glu Ala Ala Val Thr Val Thr Pro Pro Ile Thr 25 30

```
Ala Gln Gln Gly Asn Trp Thr Val Asn Lys Thr Glu Ala Asp Asn Ile
 35 40
Glu Gly Pro Ile Ala Leu Lys Phe Ser His Leu Cys Leu Glu Asp His
  50 55
                                   60
Asn Ser Tyr Cys Ile Asn Gly Ala Cys Ala Phe His His Glu Leu Glu
             70
                                75
Lys Ala Ile Cys Arg Cys Leu Lys Leu Lys Ser Pro Tyr Asn Val Cys 85 90 90
Ser Gly Glu Arg Arg Pro Leu
        100
     <210> 396
     <211> 1529
     <212> PRT
     <213> Rat
    <400> 396
Met Ser Gly Ile Gly Trp Gln Thr Leu Ser Leu Ser Leu Ala Leu Val
            5
                             10
Leu Ser Ile Leu Asn Lys Val Ala Pro His Ala Cys Pro Ala Gln Cys
20 25 30
Ser Cys Ser Gly Ser Thr Val Asp Cys His Gly Leu Ala Leu Arg Ser
  35 40
                            45
Val Pro Arg Asn Ile Pro Arg Asn Thr Glu Arg Leu Asp Leu Asn Gly
           55
                                      60
Asn Asn Ile Thr Arg Ile Thr Lys Thr Asp Phe Ala Gly Leu Arg His 65 70 75 80
Leu Arg Val Leu Gln Leu Met Glu Asn Lys Ile Ser Thr Ile Glu Arg
85 90 95
Gly Ala Phe Gln Asp Leu Lys Glu Leu Glu Arg Leu Arg Leu Asn Arg
        100 105 110
Asn Asn Leu Gln beu Phe Pro Glu Leu Leu Phe Leu Gly Thr Ala Lys
  115 120 125
Leu Tyr Arg Leu Asp Leu Ser Glu Asn Gln Ile Gln Ala Ile Pro Arg
130 135 140
Lys Ala Phe Arg Gly Ala Val Asp Ile Lys Asn Leu Gln Leu Asp Tyr 145 150 155 160
Asn Gln Ile Ser Cys Ile Glu Asp Gly Ala Phe Arg Ala Leu Arg Asp
           165 170 . 175
Leu Glu Val Leu Thr Leu Asn Asn Asn Ile Thr Arg Leu Ser Val
180 185 190
Ala Ser Phe Asn His Met Pro Lys Leu Arg Thr Phe Arg Leu His Ser 195 200 205
Asn Asn Leu Tyr Cys Asp Cys His Leu Ala Trp Leu Ser Asp Trp Leu 210 220
Arg Gln Arg Pro Arg Val Gly Leu Tyr Thr Gln Cys Met Gly Pro Ser 225 230 240
His Leu Arg Gly His Asn Val Ala Glu Val Gln Lys Arg Glu Phe Val
             245 250 255
Cys Ser Gly His Gln Ser Phe Met Ala Pro Ser Cys Ser Val Leu His
        260 - 265 270
Cys Pro Ile Ala Cys Thr Cys Ser Asn Asn Ile Val Asp Cys Arg Gly 275 280 . 285
Lys Gly Leu Thr Glu Ile Pro Thr Asn Leu Pro Glu Thr Ile Thr Glu
  290 295 300
Ile Arg Leu Glu Gln Asn Ser Ile Arg Val Ile Pro Pro Gly Ala Phe
       310
                          , 315
```

Ser	Pro	Туг	Lys	Lys 325	Leu	Arg	Arg	Leu	Asp 330	Leu	Ser	Asn	Asn	Gln 335	Ile
Ser	Glu	Leu	Ala 340	Pro	Asp	Ala	Phe	Gln 345		Leu	Arg	Ser	Leu 350	Asn	Ser
Leu	Val	Leu 355	Tyr	Gly	Asn	Lys	Ile 360		Glu	Leu	Pro	Lys 365	Ser	Leu	Phe
Glu	Gly 370	Leu	Phe	Ser	Leu	Gln 375		Leu	Leu	Leu	Asn 380	Ala	Asn	Lys	Ile
Asn 385	Сув	Leu	Arg	Val	Asp 390	Ala	Phe	Gln	Asp	Leu 3 <i>9</i> 5		Asn	Leu	Asn	Leu 400
Leu	Ser	Leu	Tyr	Asp 405	Asn	Lys	Leu	Gln	Thr 410	Val	Ala	Lys	Gly	Thr 415	
Ser	Ala	Leu	Arg 420	Ala	Ile	Gln	Thr	Met 425	His	Leu	Ala	Gln	Asn 430	Pro	Phe
		435					440					Leu 445			Asn
	450					455					460			Leu	
465					470					475				Ser	480
				485					490					Lys 495	Leu
			500					505				Lys	510		Cys
		515					520					Asn 525			Pro
	530					535					540			Asn	
545					550					555				Gln	560
				565					570					Glu 575	
			580					585				Leu	590		
		595					600					605		Ser	
	610					615					620			Asn	
625					630					635				Asp	640
	Ile			645					650			Leu		655	Leu -
Ser			660					665			_	Asn	670		Leu
		675					680					685		Gly	,
	690					695					700			Gln	_
705					710					715				Asn	720
Cys				725					730			Cys		735	Thr
Dro			740					745	_				750	Gly	
		755					760			_		765		Thr	
Val	LLO.	пλя	GTU	படிப	ser	ASII	TAT	тÄЗ	nls	ьeu	unr	пеп	тте	Asp	ьeu

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			Leu	805					810					815	
			Thr 820					825					830		
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	850		Ser			855					860				
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			Ala	885					890					895	
			Thr 900					905					910		
		915	Gln				920					925			
	930		Thr			935	_			-	940	-	_	_	
945			Gly		950					955					960
			Asn	965	*			•	970		_	•		975	
			980					985					990		
Giu	per	995	Asp	TTE	ASII	TTG	1000		Cys	GIU	ASD	1005		Cys	GTII
													_		
	1010)	Thr			1015	5				1020	Thr)	Cys		-
Pro 102	1010 Pro) Glu	Tyr	Thr	Gly 1030	1015 Glu)	Leu	Cys	Glu	Glu 1035	1020 Lys	Thr) Leu	Cys Asp	Phe	Cys 104
Pro 102: Ala	1010 Pro 5 Gln) Glu Ásp	Tyr Leu	Thr Asn 1045	Gly 1030 Pro	1015 Glu) Cys	Leu Gln	Cys His	Glu Asp 1050	Glu 1035 Ser	1020 Lys J Lys	Thr) Leu Cys	Cys Asp Ile	Phe Leu 1055	Cys 104 Thr
Pro 102: Ala Pro	1010 Pro Gln Lys) Glu Ásp Gly	Tyr Leu Phe 1060	Thr Asn 1045 Lys	Gly 1030 Pro Cys	1015 Glu) Cys Asp	Leu Gln Cys	Cys His Thr	Glu Asp 1050 Pro	Glu 1035 Ser) Gly	1020 Lys Lys Lys	Thr) Leu Cys Ile	Cys Asp Ile Gly 1070	Phe Leu 1055 Glu	Cys 104 Thr His
Pro 1029 Ala Pro Cys	1010 Pro Gln Lys Asp	Glu Ásp Gly Ile 1075	Tyr Leu Phe 1060 Asp	Thr Asn 1045 Lys Phe	Gly 1030 Pro Cys Asp	1015 Glu Cys Asp Asp	Leu Gln Cys Cys 1080	Cys His Thr 1065 Gln	Glu Asp 1050 Pro Asp	Glu 1035 Ser) Gly Asn	1020 Lys Lys Tyr	Thr) Leu Cys Ile Cys 1085	Cys Asp Ile Gly 1070 Lys	Phe Leu 1055 Glu) Asn	Cys 104 Thr His
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Pro 102: Ala Pro Cys Ala	1010 Pro Gln Lys Asp His 1090	Glu Ásp Gly Ile 1075 Cys	Tyr Leu Phe 1060 Asp	Thr Asn 1045 Lys Phe Asp	Gly 1030 Pro Cys Asp	1015 Glu Cys Asp Asp Val 1095 Cys	Leu Gln Cys Cys 1080 Asn	Cys His Thr 1065 Gln Gly	Glu Asp 1050 Pro Asp Tyr	Glu 1035 Ser) Gly Asn	1020 Lys Lys Tyr Lys Cys 1100 Pro	Thr) Leu Cys Ile Cys 1085 Val	Cys Asp Ile Gly 1070 Lys Cys	Phe Leu 1055 Glu Asn Pro	Cys 104 Thr His Gly
Pro 102: Ala Pro Cys Ala Gly 110:	1010 Pro Gln Lys Asp His 1090 Tyr	Glu Asp Gly Ile 1075 Cys Ser	Tyr Leu Phe 1060 Asp Thr	Asn 1045 Lys Phe Asp	Gly 1030 Pro Cys Asp Ala Phe 1110 Asp	1015 Glu Cys Asp Asp Val 1095 Cys	Leu Gln Cys Cys 1080 Asn Glu	Cys His Thr 1065 Gln Gly Phe	Asp 1050 Pro Asp Tyr	Glu 1035 Ser) Gly Asn Thr Pro 1115 Gln	Lys Lys Lys Lys Cys 1100 Pro	Thr Leu Cys Ile Cys 1085 Val Met	Asp Ile Gly 1070 Lys Cys Val	Phe Leu 1055 Glu Asn Pro	Cys 104 Thr His Gly Glu Leu 112 Cys
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Pro 102: Ala Pro Cys Ala Gly 110: Arg Ile Gly	1010 Pro Gln Lys Asp His 1090 Tyr Thr Ile Glu	Glu Asp Gly Ile 1075 Cys Ser Ser Arg Lys 1155	Tyr Leu Phe 1060 Asp Thr Gly Pro Val 1140 Cys	Asn 1045 Lys Phe Asp Leu Cys 1125 Asn	Gly 1030 Pro Cys Asp Ala Phe 1110 Asp Glu	1015 Glu Cys Asp Val 1095 Cys Asn Pro	Leu Gln Cys Cys 1080 Asn Glu Phe Ile Val	Cys His Thr 1065 Gln Gly Phe Asp Cys 1145 Ser	Asp 1050 Pro Asp Tyr Ser Cys 1130 Gln	Glu 1035 Ser Gly Asn Thr Pro 1115 Gln Cys	1020 Lys Lys Tyr Lys Cys 1100 Pro Asn Leu	Thr) Leu Cys Ile Cys 1085 Val) Met Gly Pro Val 1165	Cys Asp Ile Gly 1070 Lys Cys Val Ala Gly 1150 Asn	Phe Leu 1055 Glu Asn Pro Leu Gln 1135 Tyr	Cys 104 Thr His Gly Glu Leu 112 Cys Leu Glu
Pro 102: Ala Pro Cys Ala Gly 110: Arg Ile Gly Ser	1010 Pro Gln Lys Asp His 1090 Tyr Ile Glu Tyr 1170	Glu Asp Gly Ile 1075 Cys Ser Arg Lys 1155 Leu	Tyr Leu Phe 1060 Asp Thr Gly Pro Val 1140 Cys Gln	Asn 1045 Lys Phe Asp Leu Cys 1125 Asn Glu Ile	Gly 1030 Pro 5 Cys Asp Ala Phe 1110 Asp Glu Lys	1018 Glu Cys Asp Asp Val 1095 Cys Asn Pro Leu Ser 1175	Gln Cys Cys 1080 Asn Glu Phe Ile Val 1160 Ala	Cys His Thr 1065 Gly Phe Asp Cys 1145 Ser	Asp 1050 Pro Asp Tyr Ser Cys 1130 Gln Val	Glu 1038 Ser Gly Asn Thr Pro 1115 Gln Cys Asn	1020 Lys Lys Lys Tyr Lys Cys 1100 Pro Asn Leu Phe	Thr Leu Cys Ile Cys 1085 Val Met Gly Pro Val 1165 Gln	Cys Asp Ile Gly 1070 Lys Cys Val Ala Gly 1150 Asn Thr	Phe Leu 1055 Glu Asn Pro Leu 1135 Tyr Lys Asn	Cys 104 Thr His Gly Glu Leu 112 Cys Leu Glu
Pro 102: Ala Pro Cys Ala Gly 110: Arg Ile Gly Ser	1010 Pro Gln Lys Asp His 1090 Tyr Thr Ile Glu Tyr 1170 Leu	Glu Asp Gly Ile 1075 Cys Ser Arg Lys 1155 Leu	Tyr Leu Phe 1060 Asp Thr Gly Pro Val 1140 Cys	Asn 1045 Lys Phe Asp Leu Cys 1125 Asn Glu Ile	Gly 1030 Pro 5 Cys Asp Ala Phe 1110 Asp Glu Lys Pro Thr	1015 Glu Cys Asp Val 1095 Cys Asn Pro Leu Ser 1175 Asp	Gln Cys Cys 1080 Asn Glu Phe Ile Val 1160 Ala	Cys His Thr 1065 Gly Phe Asp Cys 1145 Ser	Asp 1050 Pro Asp Tyr Ser Cys 1130 Gln Val	Glu 1035 Ser) Gly Asn Thr Cgln Cys Asn Arg Gly	1020 Lys Lys Lys Tyr Lys Cys 1100 Asn Leu Phe Pro 1180 Ile	Thr Leu Cys Ile Cys 1085 Val Met Gly Pro Val 1165 Gln	Cys Asp Ile Gly 1070 Lys Cys Val Ala Gly 1150 Asn Thr	Phe Leu 1055 Glu Asn Pro Leu 1135 Tyr Lys Asn	Cys 104 Thr 5 His Gly Glu Leu 112 Cys Leu Glu Ile Lys
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Thr Asn Leu Ser Lys Gln Ser Thr Leu Asn Phe Asp Ser Pro Leu Tyr
1265 1270 1275 128
Val Gly Gly Met Pro Gly Lys Asn Asn Val Ala Ser Leu Arg Gln Ala
1285 ` 1290 1295
Pro Gly Gln Asn Gly Thr Ser Phe His Gly Cys Ile Arg Asn Leu Tyr
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                                  1310
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Tyr Ser Cys Lys Cys Leu Glu Gly His Gly Gly Val Leu Cys Asp Glu
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Val Ser Ser His Glu Gly Ser Ala Ala Asp Thr Ala Ala Glu Pro Tyr
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Phe Arg Tyr Phe Ala Thr Leu Lys Val Ile Asn Glu Pro Gly Glu Thr
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Glu Val Phe Met Thr Pro Gln Asp Phe Val Arg Ser Ile Thr Pro Asn
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Glu Lys Gln Pro Glu His Leu Gly Leu Asp Gln Tyr Ile Ile Lys Arg
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Phe Asp Gly Lys Lys Ile Ala Gln Glu Arg Glu Lys Phe Ala Asp Glu
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Lys Gly Lys Leu Thr Ile Lys Asn Phe Leu Glu Phe Gln Arg Lys Leu
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His Phe Lys Asp Gly Lys Gly Leu Thr Phe Gln Glu Val Glu Asn Phe 325 330 335
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Leu Ala Ile Lys Cys Ser Pro Ser Leu His Val Asp Asp Arg Glu Arg
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Pro Leu Pro Trp Asp Leu Arg Phe Arg Ile Val His Glu Thr Ala Val
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Gly Met Asn Phe Leu His Cys Met Ser Pro Pro Leu Leu His Leu Asp
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Ser Asp Phe Gly Leu Ala Lys Cys Asn Gly Met Ser His Ser His Asp
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Ser Phe Ala Ile Val Ile Trp Gly Val Leu Thr Gln Lys Lys Pro Phe 210 215 220
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His Val Ala Cys Gln His Gly Gln Glu Asn Ile Val Arg Thr Leu Leu
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Ala Gln Gln Gly Asn Trp Thr Val Asn Lys Thr Glu Ala Asp Asn Ile 35 40 45
Glu Gly Pro Ile Ala Leu Lys Phe Ser His Leu Cys Leu Glu Asp His
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Asn Ser Tyr Cys Ile Asn Gly Ala Cys Ala Phe His His Glu Leu Glu
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Lys Ala Ile Cys Arg Cys Phe Thr Gly Tyr Thr Gly Glu Arg Cys Leu
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40

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295

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<211> 106 <212> PRT <213> Mouse

<400> 459

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Arg Phe Pro Phe Tyr Tyr Glu Phe Lys Met Ala Phe Val Leu Trp Leu 65 70 75 80
Leu Ser Pro Tyr Thr Lys Gly Ala Ser Leu Leu Tyr Arg Lys Phe Val

Leu Ser Pro Tyr Thr Lys Gly Ala Ser Leu Leu Tyr Arg Lys Phe Val 85 90 . 95 His Pro Ser Leu Ser Arg His Glu Lys Glu Ile Asp Ala Cys Ile Val

Gln Ala Lys Glu Arg Ser Tyr Glu Thr Met Leu Ser Phe Gly Lys Arg
115 120 , 125



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Leu Glu Asp Gln Val Pro Arg Arg Pro Pro Ile Gly Tyr Arg Pro
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Gly Gly Leu Gln Gly Ser Asp Thr Glu Asp Glu Cys Trp Ser Asp Asn 200 205
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Glu Ile Val Pro Gln Pro Pro Val Gly Pro Arg Glu Lys Pro Leu Gly 210 215 220
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 Asp Pro Val Ser Tyr Val Leu Gln Val Leu Val Gly Arg Asp Ser Glu
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 Tyr Lys Gln Val Tyr Lys Gly Glu Glu Ala Thr Phe Gln Ile Ser Gly
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 Gly Met Glu Glu Ala Lys Met Lys Gly Met Met Pro Thr Asp Glu Gln
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Pro His Cys Glu Glu Lys Met Val Ile Val Thr Thr Lys Ser Met Ser
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tragtating greating greating great teagrants to the same and the same 
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Ile Lys Leu Asp Cys Arg Lys Arg Arg Asp Lys Thr Ser Leu Leu Phe
                       40 ,
```

Cys Pro Gln Gly Pro Arg Asn Pro Val Ser Lys Ala Pro His Gln Leu 50 55 5 60 60 Gln Cys Val Pro Val Ser Arg Val Pro Thr Gly Thr Glu Ser Ser Gly 65 70 70 80 Thr

<210> 491

<211> 193

<212> PRT

<213> Human

<400> 491

Met Ala Pro Leu Leu Ser Leu Ser Cys Phe Trp Ala Asn Leu Leu Ala 10 15 Ile Arg Ser Trp Leu Thr Arg Lys His Ile Gln Arg Leu His Ala Ala 20 25 30 Ala Thr Val Ile Lys Arg Ala Trp Gln Lys Trp Arg Ile Arg Met Ala . 35 40 45 Cys Leu Ala Ala Lys Glu Leu Asp Gly Val Glu Lys His Phe Ser 55 60 Gln Ala Pro Cys Ser Leu Ser Thr Ser Pro Leu Gln Thr Arg Leu 65 70 75 80 Glu Ala Ile Ile Arg Leu Trp Pro Leu Gly Leu Val Leu Ala Asn Thr 85 90 90 95 Ala Met Gly Val Gly Ser Phe Gln Arg Lys Leu Val Val Trp Ala Cys
100 105 110 Leu Gln Leu Pro Arg Gly Ser Pro Ser Ser Tyr Thr Val Gln Thr Ala 115 Gln Asp Gln Ala Gly Val Thr Ser Ile Arg Ala Leu Pro Gln Gly Ser 130 135 140 Ile Lys Phe His Cys Arg Lys Ser Pro Leu Arg Tyr Ala Asp Ile Cys 155 160 Pro Glu Pro Ser Pro Tyr Ser Ile Thr Gly Phe Asn Gln Ile Leu Leu 165 170 175 Glu Arg His Arg Leu Ile His Val Thr Ser Ser Ala Phe Thr Gly Leu 180 185 Gly

<210> 492

<211> 104

<212> PRT

<213> Human

<400> 492

Met Pro Pro Asn Pro Asn Pro His Jew Thr Jew Ile Lew Ile Thr Ala Lew Tro 15
Glu Ala Val Val Gly Gly Ser Lew Lys Pro Arg Arg Lew Arg Lew Glu 25
Cys Cys Thr Ile Ala Pro Lew His Ser Thr Ala Tro As Thr Glu Gly Asp Pro Arg Arg Lew Arg Lew Gly Asp Pro Cys Pro Arg Arg Lew Arg Lew Gly Asp Pro Cys Ilew Arg Lew Bro Lew His Ser Thr Ala Tro As Thr Glw Gly Asp Pro Cys Lys Lys Lys Arg Glw Thr Ala Val Lew Go Cys Thr Asp Pro Cys Lys Lys Lys Lys Lys Lew Cys Lew Val Lew Cys Arg Asp Rou Lew Cys Thr Cys Lew Cy

```
85
                             90
                                              95
Leu Met Pro Ser Gly Gly Leu Thr
    100
     <210> 493
     <211> 254
     <212> PRT
     <213> Human
    <400> 493
Met Ile Leu Leu Ile Ile Val Tyr Trp Asp Ser Ala Gly Ala Ala His
1 5
                     10
Phe Tyr Leu His Thr Ser Phe Ser Arg Pro His Thr Gly Pro Pro Leu
      20
                 25
                                          30
Pro Thr Pro Gly Pro Asp Arg Asp Arg Glu Leu Thr Ala Asp Ser Asp 35 40 45
Val Asp Glu Phe Leu Asp Lys Phe Leu Ser Ala Gly Val Lys Gln Ser 50 60
Asp Leu Pro Arg Lys Glu Thr Glu Gln Pro Pro Ala Pro Gly Ser Met
             70
                          75
Glu Glu Ser Val Arg Gly Tyr Asp Trp Ser Pro Arg Asp Ala Arg Arg
          85
                    90 95
Ser Pro Asp Gln Gly Arg Gln Gln Ala Glu Arg Arg Ser Val Leu Arg 100 105 110
Gly Phe Cys Ala Asn Ser Ser Leu Ala Phe Pro Thr Lys Glu Arg Ala
115 120 125
Phe Asp Asp Ile Pro Asn Ser Glu Leu Ser His Leu Ile Val Asp Asp
 130 135 140
Arg His Gly Ala Ile Tyr Cys Tyr Val Pro Lys Val Ala Cys Thr Asn 145 150 155 160
Trp Lys Arg Val Met Ile Val Leu Ser Gly Ser Leu Leu His Arg Gly
         165 170 175
Ala Pro Tyr Arg Asp Pro Leu Arg Ile Pro Arg Glu His Val His Asn
        180 185 190
Ala Ser Ala His Leu Thr Phe Asn Lys Phe Trp Arg Arg Tyr Gly Lys
195 200 205
.
Leu Ser Arg His Leu Met Lys Val Lys Leu Lys Lys Tyr Thr Lys Phe
210 215 220
Leu Phe Val Arg Asp Pro Phe Val Arg Leu Ile Ser Ala Phe Arg Ser 225 230 235 240
Lys Phe Glu Leu Glu Asn Glu Glu Phe Tyr Arg Lys Phe Ala
   245
                   250
    <210> 494
    <211> 215
    <212> PRT
    <213> Rat
    <400> 494
Met Arg Pro Val Val Pro Ile His Val Phe Ser Ser Glu Asp Ser Pro
1 5
                      10 15
Pro Arg Asp Ala Pro Ser Thr Ser Ser Val Ala Pro Ala Ser Arg Ala
      20
                Val His Thr Pro Pro Leu Gly Pro Ile Leu Lys Lys Thr Ala Gly Leu
  35
                     40
                                      45
Gly Phe Cys Ala Val Phe Leu Tyr Phe Ile Thr Ala Leu Ile Phe Pro
                   55
                                    60
```

```
Ala Ile Ser Thr Asn Ile Gln Pro Met His Lys Gly Thr Gly Ser Pro
                 70
                                   75
Trp Thr Ser Lys Phe Tyr Val Pro Leu Thr Val Phe Leu Leu Phe Asn
                               90 .
Phe Ala Asp Leu Cys Gly Arg Gln Val Thr Ala Trp Ile Gln Val Pro
    100 105 110
Gly Pro Arg Ser Lys Leu Leu Pro Ile Leu Ala Val Ser Arg Val Cys
115 120 125
Leu Val Pro Leu Phe Leu Leu Cys Asn Tyr Gln Pro Arg Ser His Leu
  130 135 140
Thr Leu Val Leu Phe Gln Ser Asp Ile Tyr Pro Ile Leu Phe Thr Cys 145 150 150 160
Leu Leu Gly Leu Ser Asn Gly Tyr Leu Ser Thr Leu Val Leu Met Tyr
           165 170 175
Gly Pro Lys Ile Val Pro Arg Glu Leu Ala Glu Ala Thr Ser Val Val
         180 185 190
Met Leu Phe Tyr Met Ser Leu Gly Leu Met Leu Gly Ser Ala Cys Ala
195 200 205
Ala Leu Leu Glu His Phe Ile
  210 215
     <210> 495
     <211> 91
     <212> PRT
     <213> Human
     <400> 495
Met Ile Gln Pro Ser Leu Ser Val Leu Cys Gly Leu Gly Cys Ala Phe
                             10
Leu Trp Ala Thr Ser Ser Phe Ala Ala Val Ser Pro Pro Ala Cys Ala 20 25 30
Pro Ala Thr Ser Pro Ser Pro Val Val His Leu Arg Ser Thr Gln Pro
    35
                     40
                             4.5
Gly Gln Ser Cys Phe Val Leu Leu His Arg Leu Gly Leu Pro Cys Val
   50 55 60
Leu Ser Ser Ser Gly Ser Phe Ser Ser Pro His Leu Phe Cys Phe Leu 65
Pro Val Leu Val Ser Pro Cys Ala Leu Gly Pro
     <210> 496
     <211> 224
     <212> PRT
     <213> Human
     <400> 496
Met Ala Ala Cys Gly Pro Gly Ala Ala Gly Tyr Cys Leu Leu
                             10
Gly Leu His Leu Phe Leu Leu Thr Ala Gly Pro Ala Leu Gly Trp Asn
   20 25 30
Asp Pro Asp Arg Met Leu Leu Arg Asp Val Lys Ala Leu Thr Leu His 35 40 45
Tyr Asp Arg Tyr Thr Thr Ser Arg Arg Leu Asp Pro Ile Pro Gln Leu
                   55
Lys Cys Val Gly Gly Thr Ala Gly Cys Asp Ser Tyr Thr Pro Lys Val 65 70 75 80
Ile Gln Cys Gln Asn Lys Gly Trp Asp Gly Tyr Asp Val Gln Trp Glu
```

```
90
Cys Lys Thr Asp Leu Asp Ile Ala Tyr Lys Phe Gly Lys Thr Val Val
100 105 110
Ser Cys Glu Gly Tyr Glu Ser Ser Glu Asp Gln Tyr Val Leu Arg Gly
115 120 125
Ser Cys Gly Leu Glu Tyr Asn Leu Asp Tyr Thr Glu Leu Gly Leu Gln
 130
           135
                             140
Lys Leu Lys Glu Ser Gly Lys Gln His Gly Phe Ala Ser Phe Ser Asp
                          155 160
145 150
Tyr Tyr Tyr Lys Trp Ser Ser Ala Asp Ser Cys Asn Met Ser Gly Leu
165 170 175
Ile Thr Ile Val Val Leu Leu Gly Ile Ala Phe Val Val Tyr Lys Leu
        180 185 190
Phe Leu Ser Asp Gly Gln Tyr Ser Pro Pro Pro Tyr Ser Glu Tyr Pro
 195 200 205
Pro Phe Ser His Arg Tyr Gln Arg Phe Thr Asn Ser Ala Gly Pro Pro
                    215
     <210> 497
     <211> 766
     <212> PRT
     <213> Rat
     <400> 497
Met Leu Leu Leu Leu Leu Leu Pro Ala Cys Pro Leu Leu Ser
 1
              5
                               10
Ala Arg Met Phe Pro Gly Asn Ala Gly Gly Glu Leu Val Thr Pro His
                          25
Trp Val Leu Asp Gly Lys Thr Trp Leu Lys Val Thr Leu Lys Glu Gln 35 40 45
Ile Ser Lys Pro Asp Ser Gly Leu Val Ala Leu Lys Ala Glu Gly Gln
  50
                 55 60
Asp Leu Leu Glu Leu Glu Lys Asn His Arg Leu Leu Ala Pro Gly 65 70 75 80
Tyr Thr Glu Thr Tyr Tyr Ser Arg Asp Gly Gln Pro Ile Val Leu Ser
85 90
Pro Asn His Thr Asp His Cys His Tyr Gln Gly Cys Val Arg Gly Phe
         100 105 110
Arg Glu Ser Trp Val Val Leu Ser Thr Cys Ser Gly Met Ser Gly Leu
 115 120
                                          125
Ile Val Leu Ser Ser Lys Val Ser Tyr Tyr Leu His Pro Trp Met Pro
130 135 140
Gly Asp Thr Lys Asp Phe Pro Thr His Lys Ile Phe Arg Val Glu Gln
145 150 155
Leu Phe Thr Trp Arg Gly Ala Arg Lys Asp Lys Asn Ser Gln Phe Lys
165 170 175
                             170 175
Ala Gly Met Ala Arg Leu Pro His Val Pro His Arg Arg Met Arg Arg 180 185 190
Glu Ala Arg Arg Ser Pro Lys Tyr Leu Glu Leu Tyr Ile Val Ala Asp
                      200 205
His Ala Leu Phe Leu Leu Gln Arg Gln Asn Leu Asn His Thr Arg Gln
                  215
                             220
Arg Leu Leu Glu Ile Ala Asn Cys Val Asp Gln Ile Leu Arg Thr Leu 225 230 235 240
Asp Ile Gln Leu Val Leu Thr Gly Leu Glu Val Trp Thr Glu Gln Asp 245 250 255
His Ser Arg Ile Thr Gln Asp Ala Asp Glu Thr Leu Trp Ala Phe Leu
```

			260					265					270		
Gln	Trp	Arg 275		Gly	Leu	Trp	Val 280		Arg	Pro	His	Asp 285		Thr	Gln
Leu	Leu 290	Thr	Gly	Arg	Thr	Phe 295	Gln	Gly	Thr	Thr	Val 300		Leu	Ala	Pro
Val 305	Glu	G1y	Met	Cys	His 310	Ala	Glu	Ser	Ser	Gly 315	Gly	Val	Ser	Thr	Asp 320
				325	Ile				330					335	
			340		Leu			345					350		
		355			Gly		360					365			
	370				Phe	375					380				
385					Gly 390					395					400
				405	Pro				410					415	
			420		Cys			425					430		_
		435			Cys		440					445	•		
	450				Arg	455		•			460		٠,		_
465					Asp 470					475					480
				485	Ala				490					495	
			500		Tyr			505					5,10		
		515			Leu		520					525			
	530				Met	535					540				
545					Gly 550					555					560
				565	Leu				570					575	
			580		Val			585					590		
		595			Ala		600			-		605			
	610				Val	615					620				
625					His 630					635		-			640
				645	Cys				650					655	
			660		Ala			665					670		
		675			Val		680					685			
	690				Ala	695					700				
705	ат.	ALG	GΤÃ	neu	Ala 710	ırp	суѕ	Tyr,	īλī	715	ьeu	rro	TIII	ьeu	Cys 720

```
Gln Pro Leu Gly Ser Val His Pro Val Glu Phe Gly Ser Ile Ile Thr 740 745 750
Gly Glu Pro Ser Pro Pro Asn Pro Glu Glu Ser Glu Leu Thr
                 760
     <210> 498
     <211> 609
     <212> PRT
     <213> Rat
     <400> 498
Met Trp Ile Thr Ala Leu Leu Leu Leu Val Leu Leu Val Val Val 15
His Arg Val Tyr Val Gly Leu Phe Thr Gly Ser Ser Pro Asn Pro Phe
  20 25
                                            3.0
Ala Glu Asp Val Lys Arg Pro Pro Glu Pro Leu Val Thr Asp Lys Glu
     35
                        40
                                          45
Ala Arg Lys Lys Val Leu Lys Gln Ala Phe Ser Val Ser Arg Val Pro
 50 55
Glu Lys Leu Asp Ala Val Val Ile Gly Ser Gly Ile Gly Gly Leu Ala 65 70 75 80
Ser Ala Ala Ile Leu Ala Lys Ala Gly Lys Arg Val Leu Val Leu Glu
85 90
             85
Gln His Thr Lys Ala Gly Gly Cys Cys His Thr Phe Gly Glu Asn Gly
100 105 110
         100
                           105
                                             110
Leu Glu Phe Asp Thr Gly Ile His Tyr Ile Gly Arg Met Arg Glu Gly 115 120 125
Asn Ile Gly Arg Phe Ile Leu Asp Gln Ile Thr Glu Gly Gln Leu Asp
 130 135 140
Trp Ala Pro Met Ala Ser Pro Phe Asp Leu Met Ile Leu Glu Gly Pro
    150 155.
Asn Gly Arg Lys Glu Phe Pro Met Tyr Ser Gly Arg Lys Glu Tyr Ile
165 170 175
Gln Gly Leu Lys Glu Lys Phe Pro Lys Glu Glu Ala Val Ile Asp Lys
         180 185 190
Tyr Met Glu Leu Val Lys Val Val Ala His Gly Val Ser His Ala Ile
195 200 205
Leu Leu Lys Phe Leu Pro Leu Pro Leu Thr Gln Leu Leu Asn Lys Phe 210 215 . 220
Gly Leu Leu Thr Arg Phe Ser Pro Phe Cys Arg Ala Ser Thr Gln Ser
225 230 235 240
Leu Ala Glu Val Leu Lys Gln Leu Gly Ala Ser Pro Glu Leu Gln Ala
245 250 255
Val Leu Ser Tyr Ile Phe Pro Thr Tyr Gly Val Thr Pro Ser His Thr 260 265 . 270
Thr Phe Ser Leu His Ala Leu Leu Val Asp His Tyr Ile Gln Gly Ala
  275 . 280 285
Tyr Tyr Pro Arg Gly Gly Ser Ser Glu Ile Ala Phe His Thr Ile Pro
   290 295
                                      300
Leu Ile Gln Arg Ala Gly Gly Ala Val Leu Thr Arg Ala Thr Val Gln 305 310 315 320
Ser Val Leu Leu Asp Ser Ala Gly Arg Ala Cys Gly Val Ser Val Lys
325 330 335
Lys Gly Gln Glu Leu Val Asn Ile Tyr Cys Pro Val Val Ile Ser Asn
                           34,5
```

```
Ala Gly Met Phe Asn Thr Tyr Gln His Leu Leu Pro Glu Ser Val Arg
 355 360 365
Tyr Leu Pro Asp Val Lys Lys Gln Leu Thr Met Val Lys Pro Gly Leu
  370
                  375
Ser Met Leu Ser Ile Phe Ile Cys Leu Lys Gly Thr Lys Glu Glu Leu
385 390 395
Lys Leu Gln Ser Thr Asn Tyr Tyr Val Tyr Phe Asp Thr Asp Met Asp 405 ^{\circ} 410 415
Lys Ala Met Glu Arg Tyr Val Ser Met Pro Lys Glu Lys Ala Pro Glu 420 420 425
His Ile Pro Leu Leu Phe Ile Ala Phe Pro Ser Ser Lys Asp Pro Thr 435 440 445
Trp Glu Asp Arg Phe Pro Asp Arg Ser Thr Met Thr Val Leu Val Pro
 450 455
                          460
Thr Ala Phe Glu Trp Phe Glu Glu Trp Gln Glu Glu Pro Lys Gly Lys
465 470 475 480
Arg Gly Val Asp Tyr Glu Thr Leu Lys Asn Thr Phe Leu Glu Ala Ser
            485 490 495
Met Ser Val Ile Met Lys Leu Phe Pro Gln Leu Glu Gly Lys Val Glu 500 505
Ser Val Thr Gly Gly Ser Pro Leu Thr Asn Gln Tyr Tyr Leu Ala Ala
515 525
His Arg Gly Ala Thr Tyr Gly Ala Asp His Asp Leu Ala Arg Leu His
 530 535 540
Pro His Ala Met Ala Ser Leu Arg Ala Gln Thr Pro Ile Pro Asn Leu
                               555
545
       550
Tyr Leu Thr Gly Gln Asp Ile Phe Thr Cys Gly Leu Met Gly Ala Leu 565 575
Gln Gly Ala Leu Leu Cys Ser Ser Ala Ile Leu Lys Arg Asn Leu Tyr
       580 585 590
Ser Asp Leu Gln Ala Leu Gly Ser Lys Val Arg Ala Gln Lys Lys
      595 600
Lys
    <210> 499
     <211> 559
     <212> PRT
    <213> Rat
    <400> 499
Phe Gly Arg Glu Asn Phe Tyr Glu Val Gln Val Pro Glu Asp Thr Pro
                        1.0
Ile Gly Ser Ser Ile Ile Thr Ile Ser Ala Lys Asp Leu Asp Met Gly
      20
                         25
Asn Tyr Gly Lys Ile Ser Tyr Ser Phe Leu His Ala Thr Glu Asp Val 35 40 45 .
Arg Lys Thr Phe Glu Ile Asn Pro Thr Ser Gly Glu Val Asn Leu Arg
 50 55 60
Ser Leu Leu Asp Phe Glu Val Ile Gln Ser Tyr Ser Val Thr Ile Gln
             70
                              75
Ala Thr Asp Gly Gly Leu Ser Ala Lys Cys Thr Leu Ser Val Lys
          85 90 · 95
Val Leu Asp Ile Asn Asp Asn Ala Pro Glu Val Ile Ile Ser Ser Val
100 105 110
Thr Lys Thr Ile Pro Glu Asn Ala Ser Glu Thr Leu Ile Thr Leu Phe
                      120 ,
```

```
Ser Val Arg Asp Gln Asp Ser Gly Asp Asn Gly Arg Ile Leu Cys Ser
  130 135 140
Ile Pro Asp Asp Leu Pro Phe Ile Leu Lys Pro Thr Phe Lys Asn Phe
145
             150
                              155
Phe Thr Leu Leu Ser Glu Lys Ala Leu Asp Arg Glu Ser Arg Ala Glu
            165
                   170
                                  175
Tyr Asn Ile Thr Ile Thr Val Ser Asp Leu Gly Thr Pro Arg Leu Thr
        180 ` 185 _ 190
Thr Gln His Thr Ile Thr Val Gln Val Ser Asp Ile Asn Asp Asn Ala 195 200 205
Pro Ala Phe Thr Gln Thr Ser Tyr Thr Met Phe Val His Glu Asn Asn
 210 215
                        220
Ser Pro Ala Leu His Ile Gly Thr Ile Ser Ala Thr Asp Ser Asp Ser
       230
                       235
Gly Ser Asn Ala His Ile Thr Tyr Ser Leu Met Pro Pro Arg Asp Pro 245 250 255
Gln Leu Ala Leu Asp Ser Leu Ile Ser Ile Asn Ala Asp Asn Gly Gln
        260 265
Leu Phe Ala Leu Arg Ala Leu Asp Tyr Glu Val Leu Gln Ala Phe Glu
 275 280
                             285
Phe Arg Val Gly Ala Thr Asp Arg Gly Ser Pro Ala Leu Ser Ser Gln 290 295 300
Ala Leu Val Arg Val Val Leu Asp Asp Asp Asp Asp Asp Ala Pro Phe
305 310 315 320
Val Leu Tyr Pro Leu Gln Asn Ala Ser Ala Pro Tyr Thr Glu Leu Leu
         325
                          330
Pro Arg Ala Ala Glu Pro Gly Tyr Leu Val Thr Lys Val Val Ala Val 340 345 350
                        345
                                350
Asp Arg Asp Ser Gly Gln Asn Ala Trp Leu Ser Phe Gln Leu Leu Lys
    355 360 365
Ala Thr Glu Pro Gly Leu Phe Ser Val Trp Ala His Asn Gly Glu Val
  370
                375
                                 380
Arg Thr Ser Arg Leu Leu Ser Glu Arg Asp Ala Pro Lys His Lys Leu
385 390 395
Leu Leu Met Val Lys Asp Asn Gly Asp Pro Pro Arg Ser Ala Ser Val
. 405 410 415
Met Leu His Val Leu Val Val Asp Gly Phe Ser Gln Pro Tyr Leu Pro
        420
                        425 430
Leu Pro Glu Val Ala His Asn Pro Ala His Asp Glu Asp Thr Leu Thr
 435
             440
Leu Tyr Leu Val Ile Ala Leu Ala Ser Val Ser Ser Leu Phe Leu Leu
 450 455 460
Ser Val Leu Leu Phe Val Gly Val Arg Leu Cys Lys Lys Ala Arg Ala
465 470
                             475
Ala Ser Leu Gly Gly Cys Ser Val Pro Glu Gly His Phe Pro Gly His
            485 490 495
Leu Val Asp Val Thr Gly Thr Gly Thr Leu Ser Gln Asn Tyr Gln Tyr 500 505 510
                        505
                                      510
Glu Val Cys Leu Thr Gly Ser Thr Gly Thr Asn Glu Phe Lys Phe Leu
    515 520 525
Lys Pro Val Met Pro Ser Leu Gln Leu Gln Asp Pro Asp Ser Asn Met
 530 535 540
Leu Val Lys Glu Asn Phe Arg Asn Ser Leu Gly Phe Asn Ile Gln
545
               550
                      555
```

<210> 500 <211> 545

<212> PRT <213> Mouse

<400> 500 Ser Leu His Phe Glu Pro Ser Lys Ile Asn Ile Phe His Lys Asp Cys 5 10 Lys Arg Asn Gly Arg Asp Ala Thr Cys Leu Ala Ala Phe Leu Cys Phe 20 25 30 Gly Pro Ile Phe Leu Ala Pro His Phe His Thr Ala Thr Val Gly Ile 35 40 35 40 45 Arg Tyr Asn Ala Thr Met Asp Glu Arg Arg Tyr Met Pro Arg Ala His 50 55 ` 60 Leu Asp Glu Gly Ala Asp Gln Phe Thr Asn Arg Ala Val Leu Leu Ser 70 Ser Gly Gln Glu His Cys Gln Arg Ile Asn Phe His Val Leu Asp Thr 85 90 95 Ala Asp Tyr Val Lys Pro Val Ala Phe Ser Val Glu Tyr Ser Leu Glu 100 105 110 Asp Pro Asp His Gly Pro Met Leu Asp Asn Gly Trp Pro Thr Thr Leu 120 125 Arg Val Ser Val Pro Phe Trp Asn Gly Cys Asn Glu Asp Glu His Cys 130 135 140Val Pro Asp Leu Val Leu Asp Ala Arg Ser Asp Leu Pro Thr Ala Met 145 150 155 160 Glu Tyr Cys Gln Gln Val Leu Arg Arg Pro Ala Gln Asp Cys Ser Ser 165 170 175 Tyr Thr Leu Ser Phe Asp Thr Thr Val Phe Ile Ile Glu Ser Thr Arg 180 185 Arg Arg Val Ala Val Glu Ala Thr Leu Glu Asn Arg Gly Glu Asn Ala 195 200 205 Tyr Ser Ala Val Leu Asn Ile Ser Gln Ser Glu Asn Leu Gln Phe Ala 210 215 220 Ser Leu Ile Gln Lys Asp Asp Ser Asp Asn Ser Ile Glu Cys Val Asn 230 235 Glu Glu Arg Arg Leu His Lys Lys Val Cys Asn Val Ser Tyr Pro Phe . 245 250 255 Phe Arg Ala Lys Ala Lys Val Ala Phe Arg Leu Asp Phe Glu Phe Ser 260 265 270 Lys Ser Val Phe Leu His His Leu Gln Ile His Leu Gly Ala Gly Ser 275 280 285 Asp Ser His Glu Gln Asp Ser Thr Ala Asp Asp Asn Thr Ala Leu Leu 290 295 300 Arg Phe His Leu Lys Tyr Glu Ala Asp Val Leu Phe Thr Arg Ser Ser 310 315 320 Ser Leu Ser His Phe Glu Val Lys Ala Asn Ser Ser Leu Glu Ser Tyr 325 330 335 Asp Gly Ile Gly Pro Pro Phe Asn Cys Val Phe Lys Val Gln Asn Leu 340 345 350 Gly Phe Phe Pro Ile His Gly Val Met Met Lys Ile Thr Val Pro Ile 355 360 365 Ala Thr Arg Gly Gly Asn Arg Leu Leu Met Leu Lys Asp Phe Phe Thr 370 375 380Arg Ser Thr Pro Thr Glu Glu Asp Leu Ser His Ala Pro Gln Arg Asn 405 410 415 His Ser Asn Ser Asp Val Val Ser Ile Ile Cys Asn Val Arg Leu Ala

```
420
                             425
                                               430
Pro Asn Gln Glu Thr Ser Phe Tyr Leu Val Gly Asn Leu Trp Leu Met 435 440 445
                                    445
Ser Leu Lys Ala Leu Lys Tyr Arg Ser Met Lys Ile Thr Val Asn Ala 450 460
Ala Leu Gln Arg Gln Phe His Ser Pro Phe Ile Phe Arg Glu Glu Asp
               470
                           475
Pro Ser Arg Gln Val Thr Phè Glu Ile Ser Lys Gln Glu Asp Trp Gln 485 490 495
Val Pro Ile Trp Ile Ile Val Gly Ser Ser Leu Gly Gly Leu Leu 500 505 510
Leu Ala Leu Leu Val Leu Ala Leu Trp Lys Leu Gly Phe Phe Lys Ser
  515 520
                                 525
Ala Lys Arg Lys Arg Glu Pro Ser Leu Gly Pro Val Pro Lys Glu Leu
  530 535
                                     540
Glu
545
     <210> 501
     <211> 696
     <212> PRT
     <213> Rat
     <400> 501
Gly Ala Pro Met Tyr Phe Ser Glu Gly Arg Glu Arg Gly Lys Val Tyr
                                10
Val Tyr Asn Leu Arg Gln Asn Arg Phe Val Phe Asn Gly Thr Leu Lys
      20
Asp Ser His Ser Tyr Gln Asn Ala Arg Phe Gly Ser Cys Ile Ala Ser 35 40 45
Val Gln Asp Leu Asn Gln Asp Ser Tyr Asn Asp Val Val Gly Ala
  50 55
                                60
Pro Leu Glu Asp Ser His Arg Gly Ala Ile Tyr Ile Phe His Gly Phe 65 70 75 80
                                 75 · 80
Gln Thr Asn Ile Leu Lys Lys Pro Val Gln Arg Ile Ser Ala Ser Glu . 85 90 95
Leu Ala Pro Gly Leu Gln His Phe Gly Cys Ser Ile His Gly Gln Leu
100 105 110
Asp Leu Asn Glu Asp Gly Leu Val Asp Leu Ala Val Gly Ala Leu Gly
    115 120 125
Asn Ala Val Val Leu Trp Ala Arg Pro Val Val Gln Ile Asn Ala Ser
                    135 140
Leu His Phe Glu Pro Ser Lys Ile Asn Ile Phe His Lys Asp Cys Lys
145 150
                                 155
Arg Asn Gly Arg Asp Ala Thr Cys Leu Ala Ala Phe Leu Cys Phe Gly 165 170 175
Pro Ile Phe Leu Ala Pro His Phe His Thr Ala Thr Val Gly Ile Arg
180 185 190
Tyr Asn Ala Thr Met Asp Glu Arg Arg Tyr Met Pro Arg Ala His Leu
   195 200 205
Asp Glu Gly Ala Asp Gln Phe Thr Asn Arg Ala Val Leu Leu Ser Ser
           215
                             220
Gly Gln Glu His Cys Gln Arg Ile Asn Phe His Val Leu Asp Thr Ala 225 230 235 240
Asp Tyr Val Lys Pro Val Ala Phe Ser Val Glu Tyr Ser Leu Glu Asp 245 250 255
Pro Asp His Gly Pro Met Leu Asp Asn Gly Trp Pro Thr Thr Leu Arg
```

			260					265					270		
		275					Gly 280					285	His		
	290					295	Arg				300				
305	•				310		Arg			315					320
				325			Val		330					335	_
			340				Leu	345				,	350		
		355					Gln 360					365			
	370					375	Asp				380				
385					390		Val			395					400
				405			Phe		410					415	
Ser			420				Gln	425					430		
		435					Ala 440					445			
	450					455	Asp	-			460				
465					470		Ala			475					480
				485			Cys		490					495	
			500				Met	505					510		
		515					Leu 520					525			
	530					535	Ile				540				
545					550		Leu			555					560
				565			Ile		570					575	
			580				Leu	585					590		
		595					Ser 600		_			605		,	
	610					615	Pro				620				
625					630		Ile			635					640
				645			Ser		650					655	
			660				Gly _	665					670		
		675			*		Trp 680	Ala	Pro	Ser	Pro ·	Lys 685	Ser	Trp	Ser
GLU	Asp 690	rro	GTI	GIU	Ala	Ser 695	Ser								*

<210> 502

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     <213> Rat
     <400> 502
Gly His Cys Asp Cys Gln Ala Gly Tyr Gly Gly Glu Ala Cys Gly Gln
             5
                              10 15
Cys Gly Leu Gly Tyr Phe Glù Ala Glu Arg Asn Ser Ser His Leu Val
      20
                             25
Cys Ser Ala Cys Phe Gly Pro Cys Ala Arg Cys Thr Gly Pro Glu Glu 35 40 45
Ser His Cys Leu Gln Cys Arg Lys Gly Trp Ala Leu His His Leu Lys 50 60
Cys Val Asp Ile Asp Glu Cys Gly Thr Glu Gln Ala Thr Cys Gly Ala
        . 70
                                   75
Asp Gln Phe Cys Val Asn Thr Glu Gly Ser Tyr Glu Cys Arg Asp Cys
85 90 95
Ala Lys Ala Cys Leu Gly Cys Met Gly Ala Gly Pro Gly Arg Cys Lys
Lys Cys Ser Arg Gly Tyr Gln Gln Val Gly Ser Lys Cys Leu Asp Val 115 120 125
Asp Glu Cys Glu Thr Val Val Cys Pro Gly Glu Asn Glu Gln Cys Glu
130 135 140
Asn Thr Glu Gly Ser Tyr Arg Cys Val Cys Ala Glu Gly Phe Arg Gln 145 150 155 160
Glu Asp Gly Ile Cys Val Lys Glu Gln Ile Pro Glu Ser Ala Gly Phe
             165 170 175
Phe Ala Glu Met Thr Glu Asp Glu Met Val Val Leu Gln Gln Met Phe
         180
                  185 190
Phe Gly Val Ile Ile Cys Ala Leu Ala Thr Leu Ala Ala Lys Gly Asp
195 200 205
Leu Val Phe Thr Ala Ile Phe Ile Gly Ala Val Ala Ala Met Thr Gly
 210 215 220
Tyr Trp Leu Ser Glu Arg Ser Asp Arg Val Leu Glu Gly Phe Ile Lys
225 230 235
Gly Arg
     <210> 503
     <211> 819
     <212> PRT
     <213> Rat
     <400> 503
Lys Ser Trp Thr Ile Ile Gln Glu Arg Leu Gln Met Asp Ser Met Val
              5
                             10
                                                 15
Ile Lys Gly Leu Asp Pro Asp Thr Asn Tyr Gln Phe Ala Val Arg Ala
      20
                  25 30
Met Asn Ala Tyr Gly Phe Ser Leu Arg Ser Gln Pro Ser Asn Thr Ile 35 40 45
Arg Thr Leu Gly Pro Gly Glu Ala Gly Ser Gly Arg Tyr Gly Pro Gly
  50
                   55
                                60
Tyr Ile Thr Asp Thr Gly Val Ser Glu Asp Asp Asp Ala Ser Glu Asp
              70
                          75 80
Glu Leu Asp Leu Asp Val Ser Phe Glu Glu Val Lys Pro Leu Pro Ala 85 90 95
```

Thr Lys Val Gly Asn Lys Lys Ser Lys Lys Thr Ser Val Ser Asn Ser

			100					105					110		
		115		Arg			120	Pro				125	Leu		
Thr	Thr 130	Val	Ala	Val	Pro	Pro 135	Thr	Pro	Ala	Gln	Arg 140	Lys	Gly	Lys	Asn
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				Gly 245					250					255	
_	_		260	Phe				265					270		
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			340	Met				345					350		
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				485 Thr					490					495	
			500	Gly				505					510		
		515		Gly			520					525			
	530			Val		535					540				
545		1	4		550	-1011	y	,	, iob	555	טעב	77.0	11011	Der	560
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Ile Leu His Pro Phe Ser Gly Ser Ile Gln Lys Ile Ile Leu Asn Asp

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Leu Met Leu Gln Asn Leu Ser Ser Leu Arg Ser Val Ser Leu Ala Gly 65 70 75 80
Asn Thr Ile Met Arg Leu Asp Asp Ser Val Phe Glu Gly Leu Glu Arg
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Phe Pro Gly Tyr Thr Gly Lys Thr Cys Ser Gln Asp Val Asn Glu Cys 85 90 95
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Ser Tyr Lys Cys Phe Cys Leu Ser Gly His Met Leu Leu Pro Asp Ala
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Cys Glu Asp Thr Ala Glu Gly Pro Arg Cys Val Cys Pro Ser Ser Gly
145 150
                              155 160
Leu Arg Leu Gly Pro Asn Gly Arg Val Cys Leu Asp Ile Asp Glu Cys
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Ala Ser Ser Lys Ala Val Cys Pro Ser Asn Arg Arg Cys Val Asn Thr
Phe Gly Ser Tyr Tyr Cys Lys Cys His Ile Gly Phe Glu Leu Lys Tyr 195 200 205
Ile Ser Arg Arg Tyr Asp Cys Val Asp Ile Asn Glu Cys Thr Leu Asn
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Lys Lys Lys Val Lys Leu Lys Asn Val Thr Pro Arg Pro Thr Ser Thr 290 295 300
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Asn Glu Ala Glu Asp Leu Asp Leu Val Tyr Ile Gln Arg Lys Glu Leu 370 380
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Ser Phe Asp Leu Gly Val Cys Asp Trp Lys Gln Asp Arg Glu Asp Asp 405 410 415
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55

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Val Asp Leu Lys Asp Leu Ilè Leu Tyr Leu Leu Gln Ala Leu Met Val
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Leu Ser Asp Ser Gln Leu Asn Leu Leu Ala Gln Ser Val Glu Met Gly
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Ile Leu Pro His Gln Val Glu Leu Val Lys Ser Ile Leu Gln Pro Asn
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Phe Lys Tyr Pro Trp Asn Ile Pro Phe Thr Val Gln Pro Gln Leu Leu
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Glu Cys Gly Leu Lys Met Glu Leu Asn Asn Pro Arg Ser Thr Trp Asp
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Pro Arg Cys Thr Gly Ser Cys Pro Phe Ser Gly Ala Cys Ala Ser Ser 145 to 150 to 155 to 160
Leu Pro Ser Pro Leu Ser Cys Pro His Ser His Ser Gly Ser Trp Gly
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Thr Trp Ser Gln Gly Arg Pro Cys Ser Ser Thr Glu Val Ala Gly Leu
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345

340

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130 135 140 Pro Cys Ser Gly Pro Leu Leu Arg Met Ala Glu Glu Ala Ala Arg Lys 145 150 155 160150 Leu Leu Pro Ala Phe Gln Thr Pro Thr Gly Met Pro Tyr Gly Thr Val 165 170 175 Asn Leu Leu His Gly Val Asn Pro Gly Glu Thr Pro Val Thr Cys Thr Ala Gly Ile Gly Thr Phe Ile Val Glu Phe Ala Thr Leu Ser Ser Leu 195 200 205 Thr Gly Asp Pro Val Phe Glu Asp Val Ala Arg Val Ala Leu Met Arg 210 215 220 Leu Trp Glu Ser Arg Ser Asp Ile Gly Leu Val Gly Asn His Ile Asp 225 230 240 Val Leu Thr Gly Lys Trp Val Ala Gln Asp Ala Gly Ile Gly Ala Gly 245 250 255 Val Asp Ser Tyr Phe Glu Tyr Leu Val Lys Gly Ala Ile Leu Leu Gln 260 265 270 Asp Lys Lys Leu Met Ala Met Phe Leu Glu Tyr Asn Lys Ala Ile Arg 275 280 285 Asn Tyr Thr His Phe Asp Asp Trp Tyr Leu Trp Val Gln Met Tyr Lys 290 295 300 Gly Thr Val Ser Met Pro Val Phe Gln Ser Leu Glu Ala Tyr Trp Pro 305 310 315 320 Gly Leu Gln Ser Leu Ile Gly Asp Ile Asp Asn Ala Met Arg Thr Phe 325 330 335Leu Asn Tyr Tyr Thr Val Trp Lys Gln Phe Gly Gly Leu Pro Glu Phe 340 345 350 Tyr Asn Ile Pro Gln Gly Tyr Thr Val Glu Lys Arg Glu Gly Tyr Pro 355 360 365 Leu Arg Pro Glu Leu Ile Glu Ser Ala Met Tyr Leu Tyr Arg Ala Thr 375 380 Gly Asp Pro Thr Leu Leu Glu Leu Gly Arg Asp Ala Val Glu Ser Ile 385 390 395 400 Glu Lys Ile Ser Lys Val Glu Cys Gly Phe Ala Thr Ile Lys Asp Leu 405 410 415 Arg Asp His Lys Leu Asp Asn Arg Met Glu Ser Phe Phe Leu Ala Glu 425

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Thr Val Lys Tyr Leu Tyr Leu Leu Phe His Pro Asn Asn Phe Ile His
  435 440
                                  445
Asn Asn Gly Ser Thr Phe Asp Ser Val Met Thr Pro His Gly Glu Cys
  450 455
Ile Leu Gly Ala Gly Gly Tyr Ile Phe Asn Thr Glu Ala His Pro Ile
465 470 480
Asp Pro Ala Ala Leu His Cys Cys Arg Arg Leu Lys Glu Glu Gln Trp
485 490 495
Glu Val Glu Asp Leu Ile Lys Glu Phe Tyr Ser Leu Arg Gln Ser Arg
500 505 510
Ser Arg Ala Gln Arg Lys Thr Val Ser Ser Gly Pro Trp Glu Pro Pro 515 520 525
Ala Gly Pro Gly Thr Leu Ser Ser Pro Glu Asn Gln Pro Arg Glu Lys 530 540
Gln Pro Ala Arg Gln Arg Ala Pro Leu Leu Ser Cys Pro Ser Gln Pro 545 555 555 5560
Phe Thr Ser Lys Leu Ala Leu Leu Gly Gln Val Phe Leu Asp Ser Ser
                565
                                    570
<210> 627
<211> 226
<212> PRT
<213> Rat
<400> 627
Arg Lys Ile Lys Asn Lys Ile Ser Ala Gln Glu Ser Arg Lys Lys
               5
                                 1.0
Lys Glu Tyr Val Glu Cys Leu Glu Lys Lys Val Glu Thr Tyr Thr Ser 20 25 30
Glu Asn Asn Glu Leu Trp Lys Lys Val Glu Thr Leu Glu Thr Ala Asn 35 40 45
Arg Thr Leu Leu Gln Gln Leu Gln Lys Leu Gln Thr Leu Val Thr Ser
 50 55
                                   60
Lys Ile Ser Arg Pro Tyr Lys Met Ala Ala Thr Gln Thr Gly Thr Cys 70 75 80
Leu Met Val Ala Ala Leu Cys Phe Val Leu Val Leu Gly Ser Leu Ala 85 90 95

Pro Cys Leu Pro Ala Phe Ser Ser Gly Ser Lys Thr Val Lys Glu Asp 100 105 110
Pro Val Ala Ala Asp Ser Val Tyr Ala Ala Ser Gln Met Pro Ser Arg
115 120 125
Ser Leu Leu Phe Tyr Asp Asp Gly Ala Gly Ser Trp Glu Asp Gly His
 130 135 140
Arg Gly Ala Leu Leu Pro Val Glu Pro Pro Glu Gly Trp Glu Leu Lys 145 150 150
Pro Gly Gly Pro Ala Glu Pro Arg Pro Gln Asp His Leu Arg His Asp
165 170 175
His Ala Asp Ser Ile His Glu Thr Thr Lys Tyr Leu Arg Glu Thr Trp 180 185 190
Pro Glu Asp Thr Glu Asp Asn Gly Ala Ser Pro Asn Phe Ser His Pro
   195 200 205
Lys Glu Trp Phe His Asp Arg Asp Leu Gly Pro Asn Thr Thr Ile Lys
                        215
                                           220.
Leu Ser
225
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<210> 628

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<211> 82
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<213> Rat
<400> 628
Pro Ile Thr Leu Ser Cys Gln Ser Gly Asn Ala Ala Ser Leu Gln Pro
 1 5
                                10
Leu His Phe Pro Pro Val Prò Pro Glu Ala Cys Pro Cys Ala Phe Arg
20 25 30
Leu Arg Pro Phe Cys Leu His Thr Gly Cys Ala Gly Cys Ser Leu Arg
 35 40 45
Ala Ala Thr Glu Gln Cys Ala Val Ala Leu Ala Pro Gln Leu Pro Ser
 50 55
                                   60
Ala Ser Arg Ala Phe Pro Pro Leu Thr Leu Cys Asn Pro Cys Val Leu
65 70
Thr Arg
<210> 629
<211> 242
<212> PRT
<213> Rat
<400> 629
Met Ala Gly Ala Gly Pro Val Leu Ser Ile Leu Gly Leu Leu Val 1 5 5 10 10 10 15
Ser Ala Leu Phe Gly Val Leu Gly Glu Arg Pro Asn Pro Asp Leu Gly 20 25
Ala His Pro Glu Arg Arg Ser Gln Val Gly Pro Gly Ala Thr Glu Pro
 35 40
                             45
Arg Arg Gln Pro Pro Pro Lys Asp Gln Arg Glu Arg Ala Arg Ala Gly 50 55 60
Ser Leu Ser Leu Gly Ala Leu Tyr Thr Ala Ala Ile Val Ala Phe Val 65 70 75 80
Leu Phe Lys Cys Leu Gln Gln Gly Pro Asp Glu Ala Ala Val Pro Arg
85 90 95
Glu Glu Lys Asn Lys Lys Ser Ser Gln Ser Glu Gln Gln Leu Val
        100 105 110
Gln Leu Thr Gln Gln Leu Ala Gln Thr Glu Glu His Leu Asn Asn Leu
115 120 125
Met Thr Gln Leu Asp Pro Leu Phe Glu Arg Val Thr Thr Leu Val Gly
 130 135 140
Thr Gln Arg Glu Leu Leu Asn Ala Lys Leu Lys Thr Ile His His Leu
145 150 155 160
Leu Gln Asp Cys Lys Pro Gly Ile Gly Val Glu Ala Pro Glu Pro Glu
165 170 175
Ala Pro Ile His Phe Pro Glu Asp Leu Gly Lys Glu Asp Gln Glu Asp
180 185 190
Ala Gly Asn Ser Gln Ala Trp Glu Glu Pro Ile Asn Trp Ser Ser Glu 195 200 205
Thr Trp Asn Leu Ala Pro Ser Trp Glu Val Glu Gln Gly Leu Arg Arg
 210 215 220
Arg Trp His Lys Thr Lys Gly Pro Ala Val Asn Gly Gly Gln Ala Leu
225
                          235
             230
Lys Val
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<211> 289
<212> PRT
<213> Rat
<400> 630
Met Ile Val Leu Leu Tyr Val Thr Ser Leu Ala Ile Cys Ala Ser Gly
             5
                                  10
Gln Pro Arg Gly Asn Gln Ala Lys Gly Glu Ser Tyr Ser Pro Arg Tyr 20 25 30
Ile Cys Ser Ile Pro Gly Leu Pro Gly Pro Pro Gly Pro Pro Gly Ala
     35
                        40
Asn Gly Ser Pro Gly Pro His Gly Arg Ile Gly Leu Pro Gly Arg Asp 50 55
Gly Arg Asp Gly Arg Lys Gly Glu Lys Gly Glu Lys Gly Thr Ala Gly 65 70 75 80
Leu Lys Gly Lys Thr Gly Pro Leu Gly Leu Ala Gly Glu Lys Gly Asp
85 90 95
Gln Gly Glu Thr Gly Lys Lys Gly Pro Ile Gly Pro Glu Gly Glu Lys
        100
                    105
                                                 110
Gly Glu Val Gly Pro Ala Gly Pro Pro Gly Pro Lys Gly Asp Arg Gly 115 120 125
Asp Gln Gly Asp Pro Gly Leu Pro Gly Val Cys Arg Cys Gly Ser Ile 130 $135$
Val Leu Lys Ser Ala Phe Ser Val Gly Ile Thr Thr Ser Tyr Pro Glu
                150
                                    155
Glu Arg Leu Pro Ile Ile Phe Asn Lys Val Leu Phe Asn Glu Gly Glu 165 170 175
His Tyr Asn Pro Ala Thr Gly Lys Phe Ile Cys Ala Phe Pro Gly Ile
180 185 190
Tyr Tyr Phe Ser Tyr Asp Ile Thr Leu Ala Asn Lys His Leu Ala Ile
  195
                       200 205
Gly Leu Val His Asn Gly Gln Tyr Arg Ile Arg Thr Phe Asp Ala Asn
                     215 220
Thr Gly Asn His Asp Val Ala Ser Gly Ser Thr Val Ile Tyr Leu Gln 225 230 235 240
Pro Glu Asp Glu Val Trp Leu Glu Ile Phe Phe Asn Asp Gln Asn Gly 245 250 255
Leu Phe Ser Asp Pro Gly Trp Ala Asp Ser Leu Phe Ser Gly Phe Leu 260
Leu Tyr Val Asp Thr Asp Tyr Leu Asp Ser Ile Ser Glu Asp Asp Glu
       275
               280
                                             285
<210> 631
<211> 213
<212> PRT
<213> Rat
<400> 631
Met Val Leu Gly Gly Cys Pro Val Ser Tyr Leu Leu Cys Gly Gln
              5
Ala Ala Leu Leu Gly Asn Leu Leu Leu His Cys Val Ser Arg
 20 25 30
Ser His Ser Phe Asn Ala Thr Ala Glu Leu Asp Leu Thr Pro Ser Gly
                        40 ,
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```
Ala Ala His Leu Glu Gly Pro Ala Ala Ser Ser Trp Glu Tyr Ser Asp
   50
                      55
Pro Asn Ser Pro Val Ile Leu Cys Ser Tyr Leu Pro Asp Glu Phe Val 70 75 80
Asp Cys Asp Ala Pro Val Asp His Val Gly Asn Ala Thr Ala Tyr Gln
             85 90 9<del>5</del>
Glu Leu Gly Tyr Gly Cys Leu Lys Phe Gly Gly Gln Ala Tyr Ser Asp
100 105 110
Val Glu His Thr Ala Val Gln Cys Arg Ala Leu Glu Gly Ile Glu Cys
115 120 125
Ala Ser Pro Arg Thr Phe Leu Arg Lys Asn Lys Pro Cys Ile Lys Tyr 130 140
Thr Gly His Tyr Phe Ile Thr Thr Leu Leu Tyr Ser Phe Phe Leu Gly
               150 155 160
Cys Phe Gly Val Asp Arg Phe Cys Leu Gly His Thr Gly Thr Ala Val 165 170 175
Gly Lys Leu Eu Thr Leu Gly Gly Leu Gly Ile Trp Trp Phe Val Asp 180 185 190
Leu Ile Leu Leu Ile Thr Gly Gly Leu Met Pro Ser Asp Gly Ser Asn
                      200
 195
                                       205
Trp Cys Thr Val Tyr
<210> 632
<211> 167
<212> PRT
<213> Rat
<400> 632
Met Ala Ser Pro Arg Thr Ile Thr Ile Val Ala Leu Ser Val Ala Leu 1 5 10 10
Gly Leu Phe Phe Val Phe Met Gly Thr Ile Lys Leu Thr Pro Arg Leu
     20
                              25
                                         30
Ser Lys Asp Ala Tyr Ser Glu Met Lys Arg Ala Tyr Lys Ser Tyr Val 35 40 45
Arg Ala Leu Pro Leu Leu Lys Lys Met Gly Ile Asn Ser Ile Leu Leu 50 60
Arg Lys Ser Ile Gly Ala Leu Glu Val Ala Cys Gly Ile Val Met Thr 65 70 75 80
Leu Val Pro Gly Arg Pro Lys Asp Val Ala Asn Phe Phe Leu Leu Leu 90 95
Leu Val Leu Ala Val Leu Phe Phe His Gln Leu Val Gly Asp Pro.-Leu 100 105 110
Lys Arg Tyr Ala His Ala Leu Val Phe Gly Ile Leu Leu Thr Cys Arg 115 120 125
Leu Leu Ile Ala Arg Lys Pro Glu Asp Arg Ser Phe Glu Lys Lys Ala
 130 135 140 -
Leu Pro Glu Ser Ala Glu Glu Gln Pro Ser Leu Tyr Glu Lys Ala Pro 145 150 155 160
                             155
Gln Gly Lys Val Lys Val Ser
               165
<210> 633
<211> 138
<212> PRT
<213> Rat
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<400> 633
Phe Ile Arg Gly Met Leu Lys Leu Ile Leu Leu Leu Phe Ser Gly
            5
                           10 ·
Ala Thr Leu Ser Ser Thr Trp Phe Thr Leu Thr Cys Leu Asn Ser Val
 20 25
                                       30
Thr His Leu Pro Leu Thr Thr Val Thr Leu Tyr Ala Ser Cys Ile Leu
    35
                      40
                                     45
Leu Gly Val Phe Leu Asn Ser Ser Val Pro Ile Phe Phe Glu Leu Phe
50 55
Val Glu Thr Val Tyr Pro Val Pro Glu Gly Ile Thr Cys Gly Val Val 65 70 75 80
Thr Phe Leu Ser Asn Met Phe Met Gly Val Leu Leu Phe Phe Val Thr
          85 90 95
Phe Tyr His Thr Glu Leu Ser Trp Phe Asn Trp Cys Leu Pro Gly Ser
      100 105 110
Cys Leu Leu Ser Leu Leu Leu Ile Leu Cys Phe Arg Glu Ser Tyr Asp
115 120 125
Arg Leu Tyr Leu Asp Val Val Val Ser Val
130 135
<210> 634
<211> 75
<212> PRT
<213> Rat
<400> 634
Met Ile Gly Asp Ile Leu Leu Phe Gly Thr Leu Leu Met Asn Ala Gly
1 5 10
Ala Val Leu Asn Phe Lys Leu Lys Lys Lys Asp Thr Gln Gly Phe Gly 20 25 30
Glu Glu Ser Arg Glu Pro Ser Thr Gly Asp Asn Ile Arg Glu Phe Leu
35
                   40
                                    45
Leu Ser Leu Arg Tyr Phe Arg Ile Phe Ile Ala Leu Trp Asn Val Phe
50 · 55
Met Met Leu Cys Met Ile Val Leu Phe Gly Ser
             70
65
<210> 635
<211> 186
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<213> Rat
<400> 635
Met Val Ala Ala Val Ala Thr Ala Trp Leu Leu Leu Trp Ala Ala Ala
                            10
Cys Thr Gln Ser Glu Gln Asp Phe Tyr Asp Phe Lys Ala Val Asn Ile
 20
                  25 . 30
Arg Gly Lys Leu Val Ser Leu Glu Lys Tyr Arg Gly Ser Val Ser Leu
   35
                    40 45
Val Val Asn Val Ala Ser Glu Cys Gly Phe Thr Asp Gln Asn Tyr Arg
                  55
                                60
Ala Leu Gln Gln Leu Gln Arg Asp Leu Gly Pro Tyr His Phe Asn Val
            70
                       75 . 80
Leu Ala Phe Pro Cys Asn Gln Phe Gly Gln Gln Glu Pro Asp Ser Asn
         85 90 95
Arg Glu Ile Glu Asn Phe Ala Arg Arg Thr Tyr Ser Val Ser Phe Pro
         100
                         105,
```

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Met Phe Ser Lys Ile Ala Val Thr Gly Thr Gly Ala His Pro Ala Phe
 115 120
                          125
Lys Tyr Leu Thr Gln Thr Ser Gly Lys Glu Pro Thr Trp Asn Phe Trp
 130
          135
                                  140
Lys Tyr Leu Val Ala Pro Asp Gly Lys Val Val Gly Ala Trp Asp Pro
             150 155
Thr Val Pro Val Glu Glu Ile Lys Pro Arg Ile Thr Glu Gln Val Met 165 170 175
Lys Leu Ile Leu Gln Lys Arg Glu Asp Leu
180 . 185
<210> 636
<211> 930
<212> PRT
<213> Rat
<400> 636
Met Pro Ser Leu Leu Ser Leu Val Leu Thr Phe Leu Ala Val Ser Ser
       5
                            10
Pro Ser Cys Cys Gln Asn Ser Asp Thr Ala Ser Pro Lys Ala Ser Asn
 20 25
Gly Ala Ser Phe Leu Trp Asn Asn Met Arg Leu Pro Glu Tyr Ile Thr
    35
                   40
Pro Ile His Tyr Asp Leu Met Ile His Ala Asn Leu Ser Thr Leu Thr
 50 55 60
Phe Trp Gly Lys Thr Glu Val Glu Ile Thr Val Ser Gln Pro Thr Ser
        70 75
Thr Ile Ile Met His Ser His Gln Leu Gln Ile Ser Lys Ala Thr Leu 85 90 95
Arg Arg Gly Ala Glu Glu Met Leu Pro Glu Glu Pro Leu Lys Leu Met
        100 105 110
Glu Tyr Ser Ala His Glu Gln Val Ala Leu Leu Thr Ala Gln Pro Leu
             120
                            125
    115
Leu Ala Gly Ser Val Tyr Thr Val Ile Ile Thr Tyr Ala Ala Asn Leu 130 135 140
Ser Glu Asn Phe His Gly Phe Tyr Lys Ser Thr Tyr Arg Thr Gln Glu
145 150 155
Gly Glu Arg Arg Ile Leu Ala Ala Thr Gln Phe Glu Pro Thr Ala Ala
           165 170 175
Arg Met Ala Phe Pro Cys Phe Asp Glu Pro Ala Leu Lys Ala Ser Phe 180 180 185 190 .
Ser Ile Lys Ile Lys Arg Asp Pro Arg His Leu Ala Ile Ser Asn Met
    195 200 205
Pro Leu Val Lys Ser Val Thr Val Ala Glu Gly Leu Ile Glu Asp His
                215
                                  220
Ser Asp Phe Lys Ser Val Ser Lys Met Thr Lys Ser Gly Val Lys Val 245 250 255
Ser Val Tyr Ala Val Pro Asp Lys Ile Asn Gln Ala Asp Tyr Ala Leu
        260
                        265 270
Asp Ala Ala Val Thr Leu Leu Glu Phe Tyr Glu Asp Tyr Phe Ser Ile
    275
             280 - 285
Pro Tyr Pro Leu Pro Lys Gln Asp Leu Ala Ala Ile Pro Asp Phe Gln 290 295 300
Ser Gly Ala Met Glu Asn Trp Gly Leu Thr Thr Tyr Arg Glu Ser Ala
                       , 315
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Leu	Leu	Tyr	Asp	Lys 325	Glu	Lys	Ser	Ser	Ala 330	Ser	Ser	Lys	Leu	Gly 335	Ile
Thr	Met	Thr	Val 340		His	Glu	Leu	Ala 345		Gln	Trp	Phe	Gly 350		Leu
Val	Thr	Met 355		Trp	Trp	Asn	Asp 360		Trp	Leu	Asn	Glu 365		Phe	Ala
Lys	Phe 370		Glu	Phe	Val	Ser 375		Thr	Val	Thr	His 380		Glu	Leu	Lys
Val 385	Glu	Glu	Tyr	Phe	Phe 390		Lys	Cys	Val	Asn 395		Met	Glu	Val	Asp
	Leu	Asn	Ser	Ser 405		Pro	Val	Ser	Thr 410		Val	Glu	Asn	Pro 415	
Gln	Ile	Arg	Glu 420		Phe	Asp	Glu	Val 425		Tyr	Glu	Lys	Gly 430		Cys
Ile	Leu	Asn 435		Leu	Arg	Asp	Tyr 440		Ser	Ala	Asp			Lys	Arg
Gly	Ile 450		Gln	Tyr	Leu	Gln 455		Tyr	Ser	Tyr		445 Asn	Thr	Lys	Asn
Glu 465	Asp	Leu	Trp	Asn	Ser		Met	Hìs	Ile	Cys 475	460 Pro	Thr	Asp	G1y	Thr 480
	Thr	Met	Asp	Gly 485		Cys	Ser	Arg	Asn 490		His	Ser	Ser	Ser 495	
Ser	His	Trp	Arg 500		Glu	۷al	Ile	Asp 505		Lys	Ser	Met	Met 510		Thr
Trp	Thr	Leu 515		Lys	Gly	Phe	Pro 520		Ile	Thr	Ile	Thr 525		Arg	Gly
Arg	Asn 530		His	Leu	Lys	Gln 535		His	Tyr	Met	Lys 540		Ser	Glu	Cys
Phe 545	Pro	Glu	Thr	Gly	Ser 550		Trp	His	Val	Pro 555		Thr	Phe	Ile	Thr 560
	Lys	Ser	Asp	Ser 565		Gln	Arg	Phe	Leu 570		Lys	Thr	Lys	Thr 575	
Val	Ile	Ile	Leu 580		Glu	Ala	Val	Glu 585	Trp	Ile	Lys	Phe	Asn 590		Gly
Met	Asn	Gly 595		Tyr	Ile	Val	His 600		$G1_{\mathbf{y}}$	Asp	Asp	Gly 605		Ala	Ser
Leu	Asn 610	Gly	Leu	Leu	Lys	Glu 615		His	Thr	Thr	Ile 620		Ser	Asn	Asp
Arg 625	Ala	Ser	Leu	Ile	Asn 630		Ala	Phe	Gln	Leu 635		Ser	Ile	G1y	Lys 640
Leu	Ser	Ile	Glu	Lys 645	Ala	Leu	Asp	Leu	Ile 650		Tyr	Leu	Lys	Asn 655	Glu
Thr	Glu	Ile	Met 660	Pro	Ile	Phe	Gln	Gly 665	Leu	Asn	Glu	Leu	Ile 670		
Tyr	Lys	Leu 675	Met	Glu	Lys	Arg	Asp 680	Met	Val	Glu	Val	Glu 685	Thr	Gln	Phe
Lys	Asp 690	Phe	Leu	Leu	Arg	Leu 695	Leu	Lys	Asp	Leu	Ile 700	Asn,	Lys	Gln	Thr
Trp 705	Thr	Asp	Glu	Gly	Ser 710	Val	Ser	Glu	Arg	Met 715	Leu	Arg	Ser	Gln	Leu 720
Leu	Leu	Leu	Ala	Cys 725	Val	His	Arg	Tyr	Gln 730		Суз	Val	Gln	Arg 735	
Glu	Arg	Tyr	Phe 740		Glu	Trp	Lys	Ala 745		Asn	Gly	Asn	Met 750		Leu
Pro	Ile	Asp 755	Val	Thr	Leu	Ala	Val 760	Phe	Ala	Va1	Gly	Ala 765	Gln	Asn	Thr
Glu	Gly	Trp	Asp	Phe	Leu	Tyr	Ser	Ľуş	Tyr	Gln	Ser	Ser	Leu	Ser	Ser

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775
Thr Glu Lys Ser Gln Ile Glu Phe Ser Leu Cys Ile Ser Gln Asp Pro 785 790 795 800
Glu Lys Leu Gln Trp Leu Leu Asp Gln Ser Phe Lys Gly Glu Ile Ile
 805 810 815
Lys Thr Gln Glu Phe Pro His Ile Leu Thr Leu Ile Gly Arg Asn Pro 820 825 830
Val Gly Tyr Pro Leu Ala Trp Lys Phe Leu Lys Glu Asn Trp Asn Lys 835 840 845
Ile Val Gln Lys Phe Glu Leu Gly Ser Ser Ser Ile Ala His Met Val
850 855 860
Met Gly Thr Thr Asn Gln Phe Ser Thr Arg Ala Arg Leu Glu Glu Val
865 870 875 880
Lys Gly Phe Phe Ser Ser Leu Lys Lys Asn Gly Ser Gln Leu Arg Cys 885 890 895
Val Gln Gln Thr Ile Glu Thr Ile Glu Glu Asn Ile Arg Trp Met Asp
900 905 910
Lys Asn Phe Asp Lys Ile Arg Leu Trp Leu Gln Lys Glu Arg Gln Glu
Leu Leu
930
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Tyr Val Leu Leu Ala Gly Met Ala Leu Gly Ile Gln Gln Arg Phe Ser
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                    25
                                          30
Pro Glu Val Leu Gly Leu Cys Ala Ser Thr Ala Leu Val Trp Val Leu 35 40 45
Met Glu Val Leu Ala Leu Leu Gly Leu Tyr Leu Ala Thr Val Arg
Ser Glu Leu Gly Thr Phe His Leu Leu Ala Tyr Ser Gly Tyr Lys Tyr 65 70 75 80
Val Gly Met Ile Leu Ser Val Leu Thr Gly Leu Leu Phe Gly Ser Asp
          85 90
Gly Tyr Tyr Val Ala Leu Ala Trp Thr Ser Ser Ala Leu Met Tyr Phe 100 105 110
Thr Val Arg Ser Leu Arg Thr Ala Ala Ser Gly Pro Asp Ser Met Gly
   115 120 125
Gly Pro Thr Pro Arg Gln His Leu Gln Leu Tyr Leu Thr Leu Gly Ala
 130 135 140
Ala Ala Phe Gln Pro Leu Ile Ile Tyr Trp Leu Thr Phe His Leu Val
        150
145
                          155
<210> 638
<211> 165
<212> PRT
<213> Rat
<400> 638
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Met Ala Arg Ala Ala Gly Ile Thr Ala Ala Ile Thr Leu Ala Leu Leu 1 5 10 15
                                  10
Gly Val Leu Ala Leu Gly Ala Gly Asp Gly Asp Phe Arg Leu Asp Asp 20 25 30
Ala Leu Glu Asp Thr Asp Lys Lys Pro Thr Pro Lys Pro Pro Thr Pro
    35 40 45
Lys Lys Pro Ser Ser Gly Asp Phe Asp Leu Glu Glu Ala Leu Thr Gly 50 55 \ 60
Gly Ala Asp Glu Asp Pro Arg Arg Pro Gly Ser Arg Pro Lys Pro Asp 65 70 75 80
Pro Lys Pro Pro Gly Pro Pro Arg Asp Ser Gly Gly Ile Ser Asp Arg 85 90 95
Asp Leu Glu Asp Val Ala Gly His Gly Gly Arg Gly Gly Gly Ala Gly 100 105 110
Asp Arg Gly Thr Asp Gly Ala Glu Ser Glu Gly Gln Pro Gln Gly Leu
115 120 125
Ile Pro Gly Val Val Ala Ala Val Leu Ala Ala Leu Ala Gly Ala Val
 130 135 140
Ser Ser Phe Val Ala Tyr Gln Lys Arg Arg Leu Cys Phe Arg Glu Gly
145 150
                          155
Gly Ser Ala Pro Val
              165
<210> 639
<211> 61
<212> PRT
<213> Rat
<400> 639
Met His Ile Tyr Lys Tyr Val His Ile Asn Tyr Tyr Leu His Leu His 1 1 	 5 	 10
The Cys Ile Tyr Val Tyr Thr His Ile Ser Val Gly Met Cys Ile Arg 20 25 30
Ile Cys Leu Pro Ser Ser Ser His Trp Lys Lys Glu Ser Ile Arg Ser
 35 40
                                   45
_ __ buys Asn Ala His
50 55
Gly Gly Ser Lys Asn Ala His Tyr Pro Gly Ser Gly Ile
<210> 640
<211> 73
<212> PRT
<213> Rat
<400> 640
Met Cys Phe Ser Leu Cys Ser Val Glu Val Phe Phe Leu Lys Gln Asn 1 5 5 10 10 10 15 15
Ser Asn Leu Leu Pro Ala His Ile Phe Ile Arg Ala Ser Pro Ile Cys 20 25 30
Ile Ile Gly Asn Glu Tyr Glu Tyr Ile Phe Met Tyr Val Cys Asn His
    35 40
                                      45
Arg Ser His Leu Tyr Leu Gly Phe Ala Ala Asp Tyr Phe Phe Pro
50 55
His His Gly Thr Gly Asn Cys Phe Gln
65
                   70
<210> 641
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<211> 442 <212> PRT <213> Rat <400> 641 Met Pro Val Leu Trp Leu Leu Leu Leu Pro Leu Pro Leu Pro Leu Leu 5 10 Ala Met Leu Cys Gln Gln Arg`Ser Pro Gly Ala Arg Pro Cys Trp Leu 20 25 30 25 Ile Ser Leu Gln His Arg Val Ala Cys Val Val Leu Ser Trp Ala Ala Ala Trp Gln Arg Arg Lys Leu Glu Gln Ser Thr Leu Asn Val Ser Gln 55 50 60 Ser Gln Gln Gln Ala Leu Met Gly Cys Leu Lys Glu Ala Gln Gly Ser 65 70 80 Cys Cys Leu Pro Arg Glu Asn Thr Asp Met Thr Thr Phe Arg Asn Leu 85 90 95 Pro Leu Thr Lys Thr Ser His Thr Gln Gln Lys Glu Ser Glu Glu Lys 100 105 110 Leu Leu Pro Pro Thr Leu Pro Gln Tyr His Gly Asp Ala Ser Leu Gln 115 120 125 Val Thr Leu Leu Gly Leu Met Thr Leu Asn Lys Ala Tyr Pro Glu Val 130 135 140 Leu Ala Pro Gly Ser Thr Ala Cys Val Thr Pro Thr Ser Pro Trp Pro 145 150 155 160 Tyr Ser Val Pro Trp Leu Gly His Ala Leu Gly Arg Val Ser Pro Ile 165 170 Gly Ala Lys Asp Ala Arg Thr Leu Leu Leu Glu Ala Leu Ile Ser Pro $180 \hspace{1.5cm} 185 \hspace{1.5cm} 190 \hspace{1.5cm}$ Gly Leu Arg Val Leu Glu Ala Arg Thr Ala Val Glu Leu Leu Asp Val 195 200 205 Phe Val Gly Leu Glu Ala Asp Gly Glu Glu Leu Ala Glu Val Ile Ala 215 220 Ser Gly Ser Leu Gly Lys Leu Pro Arg Arg Ala Ala Glu Leu Gln Glu 225 230 235 240 Ala Leu Glu Gln Gly Pro Arg Gly Leu Ala Leu Arg Leu Trp Pro Lys 245 250 255 Leu Gln Val Val Val Thr Leu Asp Ala Gly Gly Gln Ala Glu Ala Val 270 260 265 Ala Ala Leu Arg Val Leu Trp Cys Gln Gly Leu Ala Phe Phe Ser Pro 275 280 Ala Tyr Ala Ala Ser Gly Gly Val Met Ala Ile Asn Leu Trp Pro Glu 290 295 300 Gln Pro Gln Gly Ser Tyr Leu Leu Ser Pro Gly Val Pro Phe Ile Glu 310 315 320 Leu Leu Pro Ile Lys Glu Gly Thr Gln Glu Glu Ala Ala Ser Thr Leu 325 330 330 Ile Gly Thr Tyr Asn Gln Cys Pro Val Val Arg Phe Thr Cys Arg Leu 375 380 Ser Val Ala Leu Ala Gln Ala Val Gly Gln Cys Gln Gly Pro Ser Cys 405 , 410

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Trp Thr Met Ser Val Trp Arg Ala Thr Phe Trp Thr Pro Met Arg Asp
420 425 430
Pro Pro His Thr Thr Lys Cys Leu Trp Ser
435
<210> 642
<211> 65
<212> PRT
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<400> 642
Met Thr Val Cys Thr Leu Leu Val Ala Lys Ser Thr Leu Leu Ser
          5 10 15
Leu Ser Cys Leu Leu Cys Ser Leu Phe Leu Tyr Ser Val Ser Gly
20 25 30.
Ser Tyr Ser Arg Cys Pro Val Arg Trp Leu Val Cys Leu Ser Ser Gln 35 40 . 45
Leu Pro Trp Ala Thr Ser Gln Ser Leu Leu Lys Arg Lys Leu Ser Met
50 55
Asn
65
<210> 643
<211> 197
<212> PRT
<213> Rat
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Pro Arg Pro Gly Arg Ala Arg Thr Leu Arg Ser Pro Ser Gly Ser Arg 1 5 10 15
Val Val Gln Arg Pro Arg Asn Asp Gly Val Ala Ala Leu Thr Gly Ala
      20
                  25
                                       3.0
Gly Gly Cys Arg Ala Pro Arg Ala Gly Met Ala Gly Gln Phe Arg Ser
     35 40 45
Tyr Val Trp Asp Pro Leu Leu Ile Leu Ser Gln Ile Val Leu Met Gln 50 55
Thr Val Tyr Tyr Gly Ser Leu Gly Leu Trp Leu Ala Leu Val Asp Ala 65 70 75 80
Leu Val Arg Ser Asn Pro Ser Leu Asp Gln Met Phe Asp Ala Glu Ile
    85 90 95
Leu Gly Phe Ser Thr Pro Pro Gly Arg Leu Ser Met Met Ser Phe Val
Leu Asn Ala Leu Thr Cys Ala Leu Gly Leu Leu Tyr Phe Ile Arg Arg
115 120
Gly Lys Gln Cys Leu Asp Phe Thr Val Thr Val His Phe Phe His Leu
130 135 140
Leu Gly Cys Trp Leu Tyr Ser Ser Arg Phe Pro Ser Ala Leu Thr Trp
145 150 155 160
Trp Leu Val Gln Ala Val Cys Ile Ala Leu Met Ala Val Ile Gly Glu
   165 170 175
Tyr Leu Cys Met Arg Thr Glu Leu Lys Glu Ile Pro Leu Ser Ser Ala
 180
                185 190
Pro Lys Ser Asn Val
195
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			420					425					430		
Ile	Leu	Asn 435	Met	Leu	Arg	qaA	Tyr 440		Ser	Ala	Asp	Thr 445		Lys	Arg
Gly	Ile 450	Val	Gln	Tyr	Arg	Gln 455	Lys	Tyr	Ser	Tyr	Lys 460	Asn	Thr	Lys	Asn
465			Trp		470					475					480
			Asp	485					490					495	
			Arg 500					505					510		
		515	Gln				520					525			
_	530		His		_	535					540	_			
545			Thr		550					555					560
	_		Asp	565			_		570				_	575	_
			Leu 580					585					590		_
		595	Tyr				б00					605			
	610	_	Leu		_	615		•			620				_
625			Leu		630					635					640
			Glu	645					650					655	
			Met 660					665					670		
		675	Met Leu				680					685			
	690		Glu			695					700				
705			Ala		710					715					720
			Phe	725					730					735	
		_	740 Val			_	_	745			_		750		
		755	Asp				760					765			,
	770		Ser			775					780				
785		_	Gln		790					795			. ,	_	800
			Glu	805			_		810			_		815	
	•		820 Pro					825					830		
		835	Lys				840					845			
	850		Thr			855					860				
865	J-7	****	****	11011	870	FIIG	ner.	TILL,		875	432.9	cu	U_U	ביעים	880

```
Lys Gly Phe Phe Ser Ser Leu Lys Lys Asn Gly Phe Gln Leu Arg Cys
       885 890 895
Val Gln Gln Thr Ile Glu Thr Ile Glu Lys Asn Ile Arg Trp Met Asp
        900 905 910
Lys Asn Phe Asp Lys Ile Arg Leu Trp Leu Gln Lys Lys Arg Gln Glu
                     920
Leu Leu
930
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1 5
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Leu Gly Leu Leu Ala Tyr Val Ala Phe Lys Cys Trp Arg Ser Arg Lys
                    25
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                                        30
Gln Arg Gln Gln Leu Ala Lys Ala Arg Thr Val Glu Leu Gly Asp Pro
                     40
Asp Arg Asp Gln Arg His Gly Asp Ser Ser Ile Phe Val Asp Ser Pro
50
      55
                       60
His Gly Leu Glu Pro Cys Ile Pro Ser Gln Gly Pro His Ala Asp Leu 65 70 75 80
                             75
              70
Gln Arg Leu Leu Ile Leu Gly Glu Pro Ala Lys Gly Trp Gln Gly Leu 100 105 110
Ala Gly Gln Leu Gly Tyr Gln Ala Glu Ala Val Glu Thr Met Ala Cys
115 120 125
Asp Gln Asp Pro Ala Tyr Ala Leu Leu Arg Asp Trp Ala Ala Gln Glu 130 140
Gly Ser Gly Ala Thr Leu Arg Val Leu Glu Asp Ala Leu Thr Ala Ile
145 155 160
Gly Arg Glu Asp Val Val Gln Val Leu Ser Ser Pro Ala Glu Gly Cys
Ser Val Val
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Phe Cys Ile Glu Ser Phe Ile Lys Arg Leu Ile Pro Lys Lys Lys
      20 25 30
Ser Val Ala Gly Glu Ile Val Leu Ile Thr Gly Ala Gly His Gly Ile
35
             40 45
Gly Arg Leu Thr Ala Tyr Glu Phe Ala Lys Leu Asn Thr Lys Leu Val
                  55 60
Leu Trp Asp Ile Asn Lys Asn Gly Ile Glu Glu Thr Ala Ala Lys Cys 65 70 75 80
Arg Lys Leu Gly Ala Gln Val His Pro, Phe Val Val Asp Cys Ser Gln
```

```
85
                           90
Arg Glu Glu Ile Tyr Ser Ala Val Arg Lys Val Lys Glu Glu Val Gly
    100
               105
                               110
Asp Val Ser Ile Leu Val Asn Asn Ala Gly Val Val Tyr Thr Ala Asp
   115 120
                                  125
Leu Phe Ala Thr Gln Asp Pro Gln Ile Glu Lys Thr Phe Glu Val Asn
130 135 140
Val Leu Ala His Phe Trp Thr Thr Lys Ala Phe Leu Pro Ala Met Met
145 150 155
Lys Asn Asn His Gly His Val Val Thr Val Ala Ser Ala Ala Gly His 165 170 175
Thr Val Val Pro Phe Leu Leu Ala Tyr Cys Ser Ser Lys Phe Ala Ala
       180 185
                                      190
Val Gly Phe His Arg Ala Leu Thr Asp Glu Leu Ala Ala Leu Gly Cys
   195 200 205
Thr Gly Val Arg Thr Ser Cys Leu Cys Pro Asn Phe Ile Asn Thr Gly 210 215 220
Phe Ile Lys Asn Pro Ser Thr Asn Leu Gly Pro Thr Leu Glu Pro Glu
225 230 235 240
Glu Val Val Glu His Leu Met His Gly Ile Leu Thr Asn Gln Lys Met
     245 250 255
Ile Phe Val Pro Gly Ser Ile Ala Leu Leu Thr Val Leu Glu Arg Val 260 265 270
Phe Pro Glu Arg Phe Leu Asp Val Leu Lys His Arg Ile Asn Val Lys
275 280 285
Phe Asp Ala Val Val Gly Tyr Lys Asp Lys
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                           10
Leu Ile Leu Pro Gly Val Glu Ala Val Glu Ala Gly Asp Ala Ile Ala
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. 20
                25
Leu Leu Gly Val Val Leu Ser Val Thr Gly Ile Cys Ala Cys Leu
35 40
                                    45
Gly Ile Tyr Ala Arg Lys Arg Asn Gly Gln Ile
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            5
                10 15
1
Asp Cys Pro Ala Ser Ile Cys Leu Asn Gly Gly Ser Cys Arg Val Gly
      20
                25
                               . 30
Ala Lys His His Leu Glu Cys Leu Cys Pro Glu Gly Phe Ile Gly Leu
    35
                   40
Tyr Cys Glu Ser Pro Val Glu Gln Arg Thr Lys Pro Ser Ser Ile Pro
                  55
```

```
Asp Thr Pro Arg Pro Pro Arg Leu Leu Pro Leu Arg Ile Glu Pro Val
    70
                                 75
Ser Pro Thr Ser Leu Arg Val Glu Leu Gln Arg Tyr Leu Gln Gly Asn
                    90
            85
Thr Val Gln Leu Arg Ser Leu Arg Leu Thr Tyr Arg Asn Leu Ser Gly
   100 105 110
Pro Asp Lys Arg Leu Val Thr Leu Arg Leu Pro Ala Ser Leu Ala Glu
115 120 125
Tyr Thr Val Thr Gln Leu Arg Pro Asn Ala Thr Tyr Ser Ile Cys Val
130 135 140
Thr Ala Leu Gly Ala Gly Arg Thr Pro Glu Gly Glu Glu Ala Cys Gly
145 150 155 160
Glu Ala Asn Thr Pro Gln Ala Val Arg Ser Asn His Ala Pro Val Thr
          165 170 175
Gln Ala Arg Glu Gly Asn Leu Pro Leu Leu Ile Ala Pro Ala Leu Ala
      180 185 190
Ala Val Leu Leu Ala Val Leu Ala Ala Ser Gly Ala Val Tyr Cys Val
 195 200 205
Arg Arg Ala Arg Ala Ser Ser Thr Ala Gln Asp Lys Gly Gln Val Gly
 210 · 215
                                   220
Pro Gly Thr Gly Pro Leu Glu Leu Glu Gly Val Lys Val Pro Leu Glu
225 230 235 240
Pro Gly Ser Lys Ala Ser Glu Gly Gly Gly Glu Ala Leu Ser Gly Gly 245 250 255
Pro Glu Cys Glu Val Pro Leu Met Gly Tyr Pro Gly Pro Ser Leu Gln
       260 265
Gly Val Leu Pro Ala Gln Pro Tyr Ile
 275 280
<210> 649
<211> 88
<212> PRT
<213> Rat
<400> 649
Leu Gly Ser Val Ser Val Thr Thr Ile Glu Pro Cys Val Gln Val Gly 1 5 10 10 15
Ser Pro Ala Arg His Ser Leu His Pro Pro Leu Cys Ile Ser Ile Gly
         20
                        25
                                        30
Ala Thr Val Pro Tyr Phe Ala Glu Gly Ser Gly Gly Pro Val Pro Thr
 35 40
Thr Ser Ala Leu Ile Leu Pro Pro Glu Tyr Ser Ser Trp Gly Tyr Pro 50 55 60
Tyr Glu Ala Pro Pro Ser Tyr Glu Gln Ser Cys Gly Ala Gly Gly Thr
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Asp Val Gly Leu Ile Pro Gly Ser
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<400> 650
Glu Val Asp Pro Asp Leu Lys Cys Ala Leu Cys His Lys Val Leu Glu 1 5 10 15
Asp Pro Leu Thr Thr Pro Cys Gly His Val Phe Cys Ala Gly Cys Val
```

```
25
            20
Leu Pro Trp Val Val Gln Glu Gly Ser Cys Pro Ser Arg Cys Arg Gly
Arg Leu Ser Ala Lys Glu Leu Asn His Val Leu Pro Leu Lys Arg Leu 50 60
  50 55
Ile Leu Lys Leu Asp Ile Lys Cys Ala His Ala Ala Arg Gly Cys Gly 65 70 75 80
Arg Val Val Lys Leu Gln Asp Leu Pro Glu His Leu Glu Arg Cys Asp 85 90 95
Phe Ala Pro Ala Arg Cys Arg His Ala Gly Cys Gly Gln Leu Leu 100 105 110
Arg Arg Asp Val Glu Ala His Met Arg Asp Ala Cys Asp Ala Arg Pro 115 120 125
       115
Val Gly Arg Cys Gln Glu Gly Cys Gly Leu Pro Leu Thr His Gly Glu
130 140
Gln Arg Ala Gly Gly His Cys Cys Ala Arg Ala Leu Arg Ala His Asn
145 155 160
Gly Ala Leu Gln Ala Arg Leu Gly Ala Leu His Lys Ala Leu Lys Lys
       165 170 175
Glu Ala Leu Arg Ala Gly Lys Arg Glu Lys Ser Leu Val Ala Gl<br/>n Leu 180 185 190
Ala Ala Gln Leu Glu Leu Gln Met Thr Ala Leu Arg Tyr Gln Lys
195 200 205
Lys Phe Thr Glu Tyr Ser Ala Arg Leu Asp Ser Leu Ser Arg Cys Val210 \phantom{0} 215 \phantom{0} 220
Ala Ala Pro Pro Gly Gly Lys Gly Glu Glu Thr Lys Ser Val Thr Leu 225 230 235 240
Val Leu His Arg Asp Ser Gly Ser Leu Gly Phe Asn Ile Ile Gly Gly 245 250 255
Arg Pro Cys Val Asp Asn Gln Asp Gly Ser Ser Ser Glu Gly Ile Phe
        260 265 270
Val Ser Lys Ile Val Asp Ser Gly Pro Ala Ala Lys Lys Arg Pro Ala
   275 . 280
Asn Ser
  290
<210> 651
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<212> PRT
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<400> 651
Met Ala Arg Pro Arg Pro Arg Glu Tyr Lys Ala Gly Asp Leu Val Phe
            5
Ala Lys Met Lys Gly Tyr Pro His Trp Pro Ala Arg Ile Asp Glu Leu 20 25 30 .
Pro Glu Gly Ala Val Lys Pro Pro Ala Asn Lys Tyr Pro Ile Phe Phe 35 40
Phe Gly Thr His Glu Thr Ala Phe Leu Gly Pro Lys Asp Leu Phe Pro
  50 55
Tyr Lys Glu Tyr Lys Asp Lys Phe Gly Lys Ser Asn Lys Arg Lys Gly 65 70 75 80
                 70
Phe Asn Glu Gly Leu Trp Glu Ile Glu Asn Asn Pro Gly Val Lys Phe
85 90 95
Thr Gly Tyr Gln Thr Ile Gln Gln Gln Ser Ser Ser Glu Thr Glu Gly 100 105 110
Glu Gly Gly Asn Thr Ala Asp Ala Ser Ser Glu Glu Glu Gly Asp Arg
```

125

120

115

```
Val Glu Asp Gly Lys Gly Lys Arg Lys Asn Glu Lys Gly Gly Ser Lys
 130 135 140
Arg Lys Lys Ser Tyr Thr Ser Lys Lys Ser Ser Lys Gln Ser Arg Lys 145 150 155 160
Ser Pro Gly Asp Glu Asp Asp Lys Asp Cys Lys Glu Glu Glu Asn Lys
165 170 175
Ser Ser Ser Glu Gly Gly Asp Ala Gly Asn Asp Thr Arg Asn Thr Thr
 180 185 190
Ser Asp Leu Gln Lys Ala Gly Glu Gly Thr
195
                        200
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<211> 79
<212> PRT
<213> Rat
<400> 652
Met Pro Val Ala Val Gly Pro Tyr Gly Gln Ser Gln Pro Ser Cys Phe
              5
                               10
Asp Arg Val Lys Met Gly Phe Val Met Gly Cys Ala Val Gly Met Ala
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                     25
Ala Gly Ala Leu Phe Gly Thr Phe Ser Cys Leu Arg Ile Gly Met Arg
 35
                     40
                                         45
Gly Arg Glu Leu Met Gly Gly Ile Gly Lys Thr Met Met Gln Ser Gly
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                    55
                                     60
Gly Thr Phe Gly Thr Phe Met Ala Ile Gly Met Gly Ile Arg Cys
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Met Pro Val Asn Leu Gly Gln Ala Leu Gly Leu Leu Pro Phe Leu Ala
1 5 10
Lys Ala Glu Asp Ala Thr Phe Ser Gly Ser Asp Val Ile Gln Gln Arg
         20
                           25
Glu Leu Ala Asn Pro Glu Thr Ala Arg Gln Leu Phe Arg Gln Phe Arg
                     40
 35
                                       45
Tyr Gln Val Met Ser Gly Pro Gln Glu Thr Leu Arg Gln Leu Arg Lys 50 60
Leu Cys Phe Gln Trp Leu Arg Pro Glu Val His Thr Lys Glu Gln Ile
                70
                                 75
Leu Glu Ile Leu Met Leu Glu Gln Phe Leu Thr Ile Leu Pro Gly Glu
                             90 - 95
Ile Gln Met Trp Val Arg Lys.Gln Cys Pro Gly Ser Gly Glu Glu Ala 100 $105\ 
Val Thr Leu Val Glu Ser Leu Lys Gly Asp Pro Gln Lys Leu Trp Gln
     115
                                    125
                     120
Trp Ile Ser Ile Gln Val Leu Gly Gln Glu Ile Pro Phe Glu Lys Glu
          135
                                    140
Asn Ser Ala Arg Cys Arg Gly Asp Lys Val Glu Pro Ala Leu Glu Ala
                150
                         155
Glu Pro Thr Val Glu Val Val Pro Gln Asp Leu Pro Leu Gln Asn Thr
                             . 170
              165
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```
Ser Ser Ala Pro Gly Glu Leu Leu Ser His Gly Val Lys Glu Glu Ser
        180
                 185
Asp Met Glu Pro Glu Leu Ala Leu Ala Ala Ser Gln Leu Pro Ala Arg
              200
  195
                                        205
Ser Glu Glu Arg Pro Thr Arg Asp Gln Glu Val Gly Thr Ala Leu Leu
210 215 220
Pro Ser Leu Gln Glu Glu Gln Trp Arg His Leu Asp Ser Thr Gln Lys
        230
                              235
Glu Gln Tyr Trp Asp Leu Met Leu Glu Thr Tyr Gly Lys Met Val Ser 245 250 255
Gly Ala Gly Ile Ser Asn Ser Lys Pro Asp Leu Thr Asn Met Ala Glu
   260 265 270
Tyr Gly Glu Glu Leu Val Gly Leu His Leu His Ser Ala Glu Lys Met
 275 . 280
                                     285
Ala Arg Ala Pro Cys Lys Glu Asp Arg Gln Glu Asn Asp Lys Glu Asn
 290 295
                             300
Leu Asn Leu Glu Asn His Arg Asp Gln Gly Cys Leu Asp Val Phe Asp 305 310 310 320
Gln Ala Pro Gly Glu Ala Pro Pro Gln Thr Ala Leu Ser Asp Phe Phe 325 330 335
Gly Glu Ser Glu Pro His His Phe Gly Gly Glu Ser Val Pro Glu Ala
                  345
Leu Glu Asn Leu Gln Gly Glu Gly Thr Gly Ala His Leu Phe Pro His 355 360 365
Glu Arg Gly Ser Gly Lys Gln Leu Gly Gln His Ile Gln Ser Ser Ser
                  375
 370
                                  380
Ser Gly Glu Leu Ser Ala Leu Trp Leu Glu Glu Lys Arg Glu Ala Ser
        390 395
Gln Lys Gly Gln Ala Arg Ala Pro Met Ala Gln Lys Leu Pro Thr Cys
          . 405 410
Arg Glu Cys Gly Lys Thr Phe Tyr Arg Asn Ser Gln Leu Val Phe His
               425 430
         420
Gln Arg Thr His Thr Gly Glu Thr Tyr Phe His Cys Arg Ile Cys Lys
 435 440
                                      445
Lys Ala Phe Leu Arg Ser Ser Asp Phe Val Lys His Gln Arg Thr His 450 460
Thr Gly Glu Lys Pro Cys Lys Cys Asp Tyr Cys Gly Lys Gly Phe Ser
                               475
465 470
Asp Phe Ser Gly Leu Arg His His Glu Lys Ile His Thr Gly Glu Lys 485 490 495
Pro Tyr Lys Cys Pro Ile Cys Glu Lys Ser Phe Ile Gln Arg Ser Asn 500 510
Phe Asn Arg His Gln Arg Val His Thr Gly Glu Lys Pro Tyr Lys Cys
    515
                    520
                                     525
Thr His Cys Gly Lys Arg Phe Ser Trp Ser Ser Ser Leu Asp Lys His
              535 540
Gln Arg Ser His Leu Gly Lys Lys Pro Cys Pro
               550
                                 555
<21.0> 654
<211> 244
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<400> 654
Leu Ala Tyr Tyr Asn Pro Phe Tyr Phe Leu Ser Ala Ala Ala Pro Gly
              5
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Pro Gly Ala Ala Thr Ser Ala Gly Ala Thr Pro Thr Ala Val Ala Gly 20 25 30
Leu Thr Ala Arg Ala Pro His Val Gln Ala Ser Ala Arg Ala Val Pro
Val Thr Arg Val Gly Ser Ala Ala Pro Ala Arg Thr Ala Ser Asp Thr
                55
Gly Arg Gln Ala Gly Arg Glu Tyr Val Ile Pro Ser Leu Ala His Arg 65 70 75 80
                               75
Phe Met Ala Glu Met Val Asp Phe Phe Ile Leu Phe Phe Ile Lys Ala 85 90 95
Thr Ile Val Leu Ser Ile Met His Leu Ser Gly Ile Lys Asp Ile Ser
        100 105
Lys Phe Ala Met His Tyr Ile Ile Glu Glu Ile Asp Glu Asp Thr Ser
115 120 125
Leu Val Cys Phe Tyr Glu Ile Ile Cys Ile Trp Gly Ala Gly Gly Ala
145 150 155 160
Thr Pro Gly Lys Phe Leu Leu Gly Leu Arg Val Val Thr Cys Asp Thr
            165 170
                                               175
Ser Val Leu Ile Ala Pro Ser Arg Val Leu Val Ile Pro Ser Ser Asn
180 185 190
Val Ser Ile Thr Thr Ser Thr Ile Arg Ala Leu Ile Lys Asn Phe Ser
195 200 205
Ile Ala Ser Phe Phe Pro Ala Phe Ile Thr Leu Leu Phe Phe Gln His
                215
                                     220
Asn Arg Thr Ala Tyr Asp Ile Val Ala Gly Thr Ile Val Val Lys Arg
                230
                                 235
Asn Gly Val Arg
<210> 655
<211> 265
<212> PRT
<213> Rat
<400> 655
Met Gly Leu Leu Phe Leu Val Leu Leu Ser Pro Leu Ser Cys Val Leu
             5
                              10
Gly Leu Pro Phe Tyr Asn Gly Phe Tyr Tyr Ser Asn Gly Leu His Gly 20 25 30
                        25
Arg Thr Leu Gly Asn Gly Tyr Gly Glu Gly Leu Phe Asn Gly Val Lys
35
                      40
Leu Val Val Glu Thr Thr Glu Glu Ser Leu Phe Ser His Gln Gly Ala
                 55
Ser Val Thr Leu Pro Cys His Tyr His Tyr Glu Pro Ala Leu Ala Ser 65 70 75 ... 80
Pro Glu Gln Asp Val Leu Val Ala Ile Gly Gln Arg His Arg Ser Phe
         100
                          105
Gly Asp Tyr Gln Gly Arg Val Gln Leu Arg Gln Asp Lys Glu Gln Glu
     115
               120 · 125
Val Ser Leu Glu Leu Arg Asp Leu Arg Leu Glu Asp Ser Gly Arg Tyr 130 135 140
Arg Cys Glu Val Ile Asp Gly Leu Glu Asp Glu Ser Gly Leu Val Glu
                         , 155
```

```
Leu Glu Leu Arg Gly Val Val Phe Pro Tyr Gln Pro Arg Glu Gly Arg
              165
                   170
                                                 175
Tyr Gln Leu Asn Phe His Glu Ala Gln Gln Val Cys Gln Glu Gln Asp
          180
                   185 . 190
Ala Val Val Ala Thr Phe Glu Gln Leu Phe Arg Ala Trp Glu Glu Gly 195 200 205
Leu Asp Trp Cys Asn Ala Gly Trp Leu Gln Asp Ala Ser Ser Cys Arg
210 215 220
Phe Gly Thr Ser Ser Cys Arg Ile Arg His Glu Ala Cys Arg Arg Pro
   230 235
Leu Trp Cys Gly Asp Pro Arg Val Asn Pro Pro Thr Pro Cys Leu Thr 245 250 255
Arg Arg Gln Asn Leu Gln Leu Arg Thr
 260
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Ser Ala Ala Ile Ala Phe His Trp Ser Pro Leu Leu Ala Val Leu Gln
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                          25
Arg Ala Leu Ser Leu His Thr Ala His Ala Thr Lys Asp Met Asp Asn
35
                      40
                                          45
Leu Phe Gln Leu Val Arg Asn Ile Val Pro Ala Leu Thr Ser Lys Lys
50 55
His Lys Gly Gln Asp Gly Arg Ile Gly Ile Val Gly Gly Cys Gln Glu 65 70 75 80
Tyr Thr Gly Ala Pro Tyr Phe Ala Gly Ile Ser Ala Leu Lys Val Gly 85 90 95
Ala Asp Leu Thr His Val Phe Cys Ala Arg Glu Ala Ala Pro Val Ile
        100 105 . 110
Lys Ser Tyr Ser Pro Glu Leu Ile Val His Pro Val Leu Asp Ser Ser 115 120 125
Asp Ala Val Glu Glu Val Lys Lys Trp Leu Pro Arg Leu His Ala Leu
  130 135 140
Val Val Gly Pro Gly Leu Gly Arg Asp Asp Leu Leu Asn Asn Val 145 150 155
Arg Gly Ile Leu Glu Ser Thr Lys Ala Arg Asp Ile Pro Val Val Ile 165 \phantom{\bigg|}170\phantom{\bigg|}
Asp Ala Asp Gly Leu Trp Leu Ile Ala Gln Arg Pro Ala Leu Val His
180 180 190
Gly Tyr Gln Lys Ala Val Leu Thr Pro Asn His Val Glu Phe Ser Arg 195 200 205
Leu Trp Asp Ala Val Leu Ser Ser Pro Met Asp Thr Ser Asn His Ser 210 215
Gly Ser Val Leu Lys Leu Ser Gln Ala Leu Gly Asn Ile Thr Ile Val
225 230 235 240
Gln Lys Gly Glu Gln Asp Leu Ile Ser Asn Gly Gln Gln Val Leu Val
             245 250 · 255
Cys Asn Gln Glu Gly Ser Ser Arg Arg Cys Gly Gly Gln Gly Asp Leu 260 265 270
Leu Ser Gly Ser Leu Gly Val Met Ala His Trp Ala Leu Arg Ala Gly
               280 ,
```

```
Pro Glu Lys Thr Asn Gly Ser Ser Pro Leu Leu Val Ala Ala Trp Gly
290 295 300
Ala Cys Thr Leu Thr Arg Glu Cys Asn His Leu Ala Phe Gln Lys Tyr
      310 315
Gly Arg Ser Thr Thr Thr Asp Met Ile Ala Glu Val Gly Ala Ala
     325
                   330
Phe Ser Lys Leu Phe Thr Thr
        340
<210> 657
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Met Pro Cys Trp Ser Leu Tyr Gln Leu Met Val Leu Tyr Gln Ile Ile
        5 10
Ile Leu Phe Phe Leu Phe Lys Gln Val Ser Val Arg Thr Cys Tyr Leu
20 25
                              30
Ser Thr Glu Gly Lys Pro Cys Gly Ser Val Leu Phe Ala Cys Lys Ser
35 40 45
Leu Gln Gln Cys Leu Leu Thr Val Leu Val Thr Pro Val
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Met Leu Trp Ala Leu Ala Leu Ala Leu Gly Ile Gly Pro Arg Ala
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                           10
                                         15
Tyr Ala Gly Asp His Gly Glu Asp Thr Ala Phe Asp Leu Phe Ser Ile
  20
                 25
Ser Asn Ile Asn Arg Lys Thr Ile Gly Ala Lys Gln Phe Arg Gly Pro
. 35 40
                                    45
Asp Pro Gly Val Pro Ala Tyr Arg Phe Val Arg Phe Asp Tyr Val Pro
· 50 55
                                  60
Pro Val Asn Thr Asp Asp Leu Asn Arg Ile Val Lys Leu Ala Arg Arg
            70
                            75 80
Lys Glu Gly Phe Phe Leu Thr Ala Gln Leu Lys Gln Asp Arg Lys Ser
85 90 95
                           90
Arg Gly Thr Leu Leu Val Leu Glu Gly Pro Gly Thr Ser Gln Arg Gln
        100 105 . 110
Phe Glu Ile Val Ser Asn Gly Pro Gly Asp Thr Leu Asp Leu Asn Tyr
                            125
    115 120
Trp Val Glu Gly His Gln His Thr Asn Phe Leu Glu Asp. Val Gly Leu 130 135 140
Ala Asp Ser Gln Trp Lys Asn Val Thr Val Gln Val Ala Ser Asp Thr 145 150 155 160
Tyr Ser Leu Tyr Val Gly Cys Asp Leu Ile Asp Ser Val Thr Leu Glu
165 170 175
Glu Pro Phe Tyr Glu Gln Leu Glu Ala Asp Lys Ser Arg Met Tyr Val
        180 185 190
Ala Lys Gly Ala Ser Arg Glu Ser His Phe Arg Gly Leu Leu Gln Asn
     195 200 205
Val His Leu Val Phe Ala Asp Ser Val Glu Asp Ile Leu Ser Lys Lys
```

	210					215					220				
Gly 225	Cys	Gln	His	Ser	Gln 230	Gly	Ala	Glu	Val	Asn 235		Ile	Ser	Glu	His 240
Thr	Glu	Thr	Leu	His 245	Leu	Ser	Pro	His	Ile 250	Thr	Thr	Asp	Leu	Val 255	Val
	Gly		260					265					270		
Leu	Ser	Asn 275	Met	Met	Asn	Glu	`Leu 280	Ser	Gly	Leu	His	Va1 285	Met	Val	Asn
	Leu 290		_			295					300				
305	Glu				310					3,15					320
	Gln		_	325					330	Glu				335	
	Cys		340					345					350		
	Thr	355					360					365			_
	Cys 370					375				_	380	-		_	_
385	Pro				390					395					400
Thr	Gln			405					410					415	
GIY		Ser	420					425					430		
	Ile	435					440					445		Ser	
-	Ser 450				_	455	_				460		_		
465	Ser				470					475					480
Arg	Glu			485					490					495	
Clar	Ile	Pro	500					505					510		
_	Gly	515		_			520	_				525			-
_	530 Arg	_	_			535	_				540			-	
545	Ala				550					555					560
Cys		Val		565					570					575	•
_	Cys		580					585					590		_
	Cys	595					600					605			
	610 Tyr					615					620				
625	Glu				630	•				635					640
	Asn			645					650					655	
	-10-1	-1.0	660	_,,	111.0	1114	u	665,		T X T		213	670	1113	201

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Asp Pro Met Tyr Lys Cys Glu Cys Gln Thr Gly Tyr Ala Gly Asp Gly 675 680 685
Leu Ile Cys Gly Glu Asp Ser Asp Leu Asp Gly Trp Pro Asn Ser Asn 690 700
Leu Val Cys Ala Thr Asn Ala Thr Tyr His Cys Val Lys Asp Asn Cys
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Pro Lys Leu Pro Asn Ser Gly Gln Glu Asp Phe Asp Lys Asp Gly Ile
725 730 735
Gly Asp Ala Cys Asp Glu Asp Asp Asp Asp Asp Gly Val Ser Asp Glu 740 · 745 · 745
Lys Asp Asn Cys Pro Leu Leu Phe Asn Pro Arg Gln Leu Asp Tyr Asp
     755 760 765
Lys Asp Glu Val Gly Asp Arg Cys Asp Asn Cys Pro Tyr Val His Asn 770 780
Gln Ala Gln Ile Asp Thr Asp Asn Asn Gly Glu Gly Asp Ala Cys Ser 785 790 795 800
Val Asp Ile Asp Gly Asp Asp Val Phe Asn Glu Arg Asp Asn Cys Pro805 \hspace{0.5cm} 810 \hspace{0.5cm} 815 \hspace{0.5cm}
Tyr Val Tyr Asn Thr Asp Gln Arg Asp Thr Asp Gly Asp Gly Val Gly 820 825 830
Asp His Cys Asp Asn Cys Pro Leu Met His Asn Pro Asp Gln Met Asp 835 840 840
Gln Asp Asn Asp Leu Val Gly Asp Gln Cys Asp Asn Asn Glu Asp Ile 850 \phantom{\bigg|} 850 \phantom{\bigg|} 850 \phantom{\bigg|} 860 \phantom{\bigg|}
Asp Asp Asp Gly His Gln Asn Asn Gln Asp Asn Cys Pro Tyr Ile Ser
                 1870
                                        875
Asn Ser Asn Gln Ala Asp His Asp Asn Asp Gly Lys Gly Asp Ala Cys
                885 890 895
Asp Ser Asp Asp Asp Asn Asp Gly Val Pro Asp Asp Asp Asp Asn Cys 900 905 910
Arg Leu Val Phe Asn Pro Asp Gln Lys Asp Ser Asp Gly Asp Gly Arg 915 920 925
Gly Asp Ile Cys Lys Asp Asp Phe Asp Asn Asp Asn Val Pro Asp Ile
 930 935
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Asp Asp Val Cys Pro Glu Asn Asn Ala Ile Thr Glu Thr Asp Phe Arg 945 950 955 960
Asn Phe Gln Met Val Pro Leu Asp Pro Lys Gly Thr Thr Gln Ile Asp
965 970 975
Pro Asn Trp Val Ile Arg His Gln Gly Lys Glu Leu Val Gln Thr Ala
 980 985 990
Asn Ser Asp Pro Gly Ile Ala Val Gly Phe Asp Glu Phe Gly Ser Val 995 \phantom{\bigg|} 1000 \phantom{\bigg|} 1005 \phantom{\bigg|}
Asp Phe Ser Gly Thr Phe Tyr Val Asn Thr Asp Arg Asp Asp Asp Tyr 1010 1015 1020
Ala Gly Phe Val Phe Gly Tyr Gln Ser Ser Ser Arg Phe Tyr Val Val
1025 1030 1035 104.0
Met Trp Lys Gln Val Thr Gln Thr Tyr Trp Glu Asp Lys Pro Ser Arg
1045 1050 1055

Ala Tyr Gly Tyr Ser Gly Val Ser Leu Lys Val Val Asn Ser Thr Thr
1060 1065 1070
Gly Thr Gly Glu His Leu Arg Asn Ala Leu Trp His Thr Gly Asn Thr 1075 1080 1085
Glu Gly Gln Val Arg Thr Leu Trp His Asp Pro Lys Asn Ile Gly Trp 1090 1095 1100
Lys Asp Tyr Thr Ala Tyr Arg Trp His Leu Ile His Arg Pro Lys Thr
1105 1110 1115 1120
Gly Tyr Met Arg Val Leu Val His Glu Gly Lys Gln Val Met Ala Asp
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1125
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Ser Gly Pro Ile Tyr Asp Gln Thr Tyr Ala Gly Gly Arg Leu Gly Leu 1140 1145 1150
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  35
              40
Ala Val Leu Arg Cys Gln Ser Pro Arg Met Val Trp Thr Gln Asp Arg 50 55
Leu His Asp Arg Gln Arg Val Val His Trp Asp Leu Ser Gly Gly Pro 65 70 75 80
Gly Ser Gln Gly Arg Arg Leu Val Asp Met Tyr Ser Ala Gly Glu Gln
                              90
Arg Val Tyr Gln Pro Arg Asp Arg Asp Arg Leu Leu Ser Pro Ser
         100 105 110
Ala Phe His Asp Gly Asn Phe Ser Leu Leu Ile Arg Ala Val Glu Arg
115 120 125
Gly Asp Glu Gly Val Tyr Thr Cys Asn Leu His His His Tyr Cys His
 130
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                                   140
Leu Tyr Glu Ser Leu Ala Val Arg Leu Glu Val Thr Asp Asp Pro Leu
145 150 155
Leu Ser Arg Ala Tyr Trp Asp Gly Glu Lys Glu Val Leu Val Val Ala 165 170 175
Leu Gly Ala Pro Ala Leu Met Thr Cys Val Asn Arg Glu His Leu Trp
180 185
                                          190
Thr Asp Arg His Leu Glu Glu Ala Gln Gln Val Val His Trp Asp Arg
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Gln Leu Pro Gly Val Pro His Asp Arg Ala Asp Arg Leu Leu Asp Leu 210 215 220
Tyr Ala Ser Gly Glu Arg Arg Ala Tyr Gly Pro Pro Phe Leu Arg Asp
225 230
                                 235
Arg Val Ser Val Asn Thr Asn Ala Phe Ala Arg Gly Asp Phe Ser Leu
           245 250 255
Arg Ile Asp Asp Leu Glu Pro Ala Asp Glu Gly Ile Tyr Ser Cys His
260 265 270
Leu His His His Tyr Cys Gly Leu His Glu Arg Arg Val Phe His Leu
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Arg Val Thr Glu Pro Val Phe Glu Pro Pro Ala Arg Ala Ser Pro Gly 290 295 300
Asn Gly Ser Gly His Asn Ser Val Pro Ser Pro Asp Pro Thr Met Ala 305 310 5310 5320
Arg Gly His Ser Ile Ile Asn Val Ile Val Pro Glu Asp His Thr His
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Phe Phe Gln Gln Leu Gly Tyr Val Leu Ala Thr Leu Leu Phe Ile
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345
          340
Leu Leu Ieu Ile Thr Val Val Leu Ala Thr Arg His Arg His Ser Gly
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              360
Gly Cys Lys Thr Ser Asp Arg Lys Ala Gly Lys Ser Lys Gly Lys Asp 370 \hspace{1cm} 375 \hspace{1cm} 380
Val Asn Met Met Glu Phe Ala Ile Ala Thr Arg Asp Gln Ala Pro Tyr
385 390 395 400
Arg Thr Glu Asp Ile Gln Leu Asp Tyr Lys Asn Asn Ile Leu Lys Glu
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Asp Lys Glu Phe Arg Lys Glu Tyr Cys Lys
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His Thr Phe Ile Ala Ser Ser Thr Val Leu Pro Gly Lys Val Gln Ala
 50 55 60
Pro Phe Ser Arg Val Leu Gln Leu Val Arg Gly Arg Ala Ser Ser Pro 65 70 75 80
Lys Leu Met Thr Leu Trp Gly Ala Phe Pro Pro Ala Arg Gly Asp Glu
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Val Leu Gly Arg Gly Trp Asn Ile Thr Ser Val Pro Leu Pro Ser His
         100 105 110
Ser Arg Gln Val Ala Gly Ser Ala Ser His Thr His Thr Leu Gly Ala
115 120 125
Ala Ser Pro Thr Pro Leu Ser Pro Gly Pro Ala Pro Leu Cys Ser Thr
· 130 135 140
Val Pro Ala Leu Pro Ser Ala Ala Thr Gly Glu Gly Trp Gly Gln Val 165 170 175 .
Ser Arg Gly Pro His Pro Val Arg Asp Gly Val Val His Ile Pro Trp
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Thr Cys Thr Trp Cys Leu Met Ala Ala Pro Thr Arg Asn Thr Pro Met 195 200 205 .
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Ala Ile Gly Cys Pro Gln Arg His Gln Leu Pro Ala Leu Gln Glu Ala
. 35
 • 35
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Thr Ala Phe Ala Gly Val His Arg Pro Leu Gln Ile His Pro Leu Gly
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Arg Gly Leu Arg Pro Trp Glu Gln Gln Gln Arg His Cys Gly His 65 70 75 80
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    35 40
Ser Asn Lys Ser Ile Arg Thr Pro Glu Pro Val Val Gln Thr Gly Pro
 50 55
                           60
Glu Phe His Pro Ser Thr Ser Ser Glu Gln Ser Asp Thr Pro Glu Pro 65 70 75 80
                              75
Val Ser Thr Thr Pro Ala Leu Gln Pro Ser Thr Ser Lys Gln Pro
100 105 110
Thr Pro Lys Pro Thr Ala Leu Val Thr Arg Gly Arg Thr His Lys Pro
115 120 125
Ser Thr Glu Gly Leu Glu Ser Val Gly Pro Val Ala Pro Asp Phe Glu
 130 135 140
Pro Pro Thr Ser Thr Asp His Leu Ala Thr Ser Lys Val Thr Gly Gln
              150
                                 155
Ser Leu Thr Leu Gln Ser Ser Pro Val Ser Ala Ser Pro Val Ser Thr
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Thr Pro Glu Leu Lys Pro Pro Val Pro Ile Ala Gln Pro Leu Thr Leu
180 185 190
Glu Pro Val Pro Gln Thr Ser His Gln Arg Arg Arg Ala Thr Gly
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Lys Gln Gly Ser Arg Thr Ala Pro Val Gly Pro Lys Ser Tyr Ser Thr.
210 215 220 --
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225 230 235 240
Ser Glu Ala Asp Ser Pro His Gln Lys Arg Pro Arg Arg Gln Val Thr
            245 250 255
Gln Lys Thr Val Val Val Lys Glu Glu Asp Pro Gly Glu Ile Gln Val
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Lys Glu Glu Pro Gln Glu Thr Ala Ile Ser Thr Pro Gly Lys Arg Lys
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Arg Asp Pro Ala Glu Gly Glu Thr Gln Gly Asn Pro Thr Arg Ser Arg
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295

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Gly Val Val Asp Ser Arg Gly Glu Arg Ala Val Leu Ala Leu Gly Gly 325 330 335
Ser Leu Ala Ser Ser Val Asn Glu Ala Ser His Leu Val Thr Asp Arg
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Ile Arg Arg Thr Val Lys Phe Leu Cys Ala Val Gly Lys Gly Ile Pro
355 360 365

Ile Leu Ser Leu Asn Trp Leu Tyr Gln Ser Arg Lys Ala Gly Cys Phe
370 375 380
Leu Pro Pro Asp Asp Tyr Leu Val Thr Asp Pro Glu Gln Glu Lys Asn
385 390 395
Phe Ser Phe Ser Leu Arg Asp Ser Leu Ser Arg Ala Arg Glu Arg Arg
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Leu Leu Glu Asp Tyr Glu Ile His Val Thr Pro Gly Val Gln Pro Pro
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Pro Pro Gln Met Gly Glu Ile Ile Ser Cys Cys Gly Gly Thr Val Leu 435 440 445
Pro Ser Met Pro His Ser Tyr Lys Leu His Arg Val Val Ile Thr Cys
 450 455 460
Thr Glu Asp Leu Pro Arg Cys Ala Ile Ala Ser Arg Leu Gly Leu Pro
465 470 475
Leu Leu Ser Pro Glu Phe Leu Leu Thr Gly Val Leu Lys Gln Glu Ala
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Lys Lys Lys Lys
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1 5 10
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                                                30
Leu Gln Trp Val Pro Gly Ser Asp Gly Ala Ser Pro Ile Arg Tyr Phe 35 40 45
                                   45
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Thr Val Gln Val Arg Glu Leu Pro Gly Gly Glu Trp Gln Thr Tyr Ser 50 60
Ser Ser Ile Ser His Glu Ala Thr Leu Cys Ala Val Glu Arg Leu Arg
65 70 75
Pro Phe Thr Ser Tyr Lys Leu Arg Leu Lys Ala Thr Asn Asp Ile Gly- 85 90 - 95
Asp Ser Asp Phe Ser Ala Glu Thr Glu Ala Val Thr Thr Leu Gln Asp 100 105 110
Val Pro Gly Glu Pro Pro Gly Ser Val Ser Ala Thr Pro His Thr Thr
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Ser Ser Val Leu Ile Gln Trp Gln Pro Pro Arg Asp Glu Ser Leu Asn 130 135 140 .
Gly Leu Gln Gly Tyr Arg Ile Tyr Tyr Arg Glu Leu Glu Ser Glu 145 150 155 160
Thr Gly Leu Ser Pro Glu Pro Lys Thr Leu Lys Ser Pro Ser Ala Leu
             165
                               170
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Arg	Ala	Glu	Leu 180	Thr	Ala	Gln	Ser	Ser 185	Phe	Lys	Thr	Val	Asn 190	Ser	Ser
Ser		195					200					205		Arg	
Tyr	Glu 210	Val	Ile	Met	Thr	Ala 215	Tyr	Asn	Ile	Ile	Gly 220	Glu	Ser	Pro	Ala
Ser 225	Val	Pro	Val	Glu	Val 230	Phe	Val	Gly	Glu	Ala 235	Ala	Pro	Ala	Met	Ala 240
Pro	Gln	Asn	Ile	Gln 245	Val	Thr	Pro	Leu	Thr 250		Ser	Gln	Leu	Glu 255	
Thr	Trp	Asp	Pro 260	Pro	Pro	Pro	Glu	Ser 265	Gln	Asn	Gly	Asn	Ile 270	Gln	Gly
Tyr	Lys	Val 275	Tyr	Tyr	Trp	Glu	Ala 280	Asp	Ser	Arg	Asn	Glu 285	Thr	Glu	Lys
Met	Lys 290	Val	Leu	Phe	Leu	Pro 295		Pro	Val	Val	Lys 300		Lys	Asp	Leu
Thr 305	Ser	His	Thr	Lys	Tyr 310	Leu	Val	Ser	Ile	Ser 315		Phe	Asn	Ala	Ala 320
Gly	Asp	Gly	Pro	Arg 325	Ser	Asp	Pro	Cys	Gln 330	Gly	Arg	Thr	His	Gln 335	Ala
Ala	Pro	Gly	Pro 340	Pro	Ser	Phe	Leu	Glu 345		Ser	Glu	Ile	Thr 350	Ser	Thr
Thr	Leu	Asn 355	Val	Ser	Trp	Gly	Glu 360	Pro	Ser	Ala	Ala	Asn 365	Gly	Ile	Leu
Gln	Gly 370	Tyr	Arg	Val	Val	Tyr 375	Glu	Pro	Leu	Ala	Pro 380	Val	Gln	Gly	Val
Ser 385	Lys	Val	Val	Thr	Val 390	qzA	Val	Lys	Gly	Asn 395	Trp	Gln	Arg	Trp	Leu 400
Lys	Val	Arg	Asp	Leu 405	Thr	Lys	Gly	Val	Thr 410	Tyr	Phe	Phe	Arg	Val 415	Gln
Ala	Arg	Thr	Ile 420	Ala	Tyr	Gly	Pro	Glu 425	Leu	Gln	Ala	Asn	Val 430	Thr	Ala
Gly	Pro	Ala 435	Glu	Gly	Ser	Pro	Gly 440	Ser	Pro	Arg	Asn	Val 445	Leu	Val	Thr
Lys	Ser 450	Ala	Ser	Glu	Leu	Thr 455	Leu	Gln	Trp	Thr	Glu 460	Gly	Asn	Thr	Gly
Asn 465	Thr	Pro	Thr	Thr	Gly 470	Tyr	Val	Ile	Glu	Ala 475	Arg	Pro	Ser	qaA	Glu 480
Gly	Leu	Trp	Asp	Met 485	Phe	Ala	Lys	Asp	Ile 490	Pro	Arg	Ser	Ala	Thr 495	Ser
Tyr	Thr	Val	Gly 500	Leu	Asp	Lys	Leu	Arg 505	Gln	Gly	Val	Thr	Tyr 510	Glu	Phe
Arg		515				_	520	_		_		525		Arg	
Ser	530					535					540			Glu	,
Trp 545					550					555				Leu	560
Val	Val	Phe	Val	Leu 565	Val	Leu	His	Gly	Gln 570	Ser	Lys	Lys	Tyr	Lys 575	Asn
Cys			580	_	_			585					590	Thr	
Asp		595			Ala	Ala	Leu 600	Glu	Leu	Asn	Ser	Arg 605	His	Leu	Asn
	Lys 610					615					620			Pro	
Pro	Ser	Pro	Gly	Gly	Leu	His	Tyr	Ser	Asp	Glu	Asp	Ile	Cys	Asn	Lys

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Tyr Asn Gly Ala Val Leu Thr Glu Ser Val Asn Leu Lys Glu Lys Ser
645 650 655
Val Asp Gly Ser Glu Ser Glu Ala Ser Asp Ser Asp Tyr Glu Glu Ala
       660 665 670
Leu Pro Lys His Ser Phe Val Asn His Tyr Met Ser Asp Pro Thr Tyr 675

Tyr Asn Phe Trp Lys Arg Arg Pro Pro Ala Ala Ala Pro His Arg Tyr
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                                              30
Val Gly Ser Asp Val Glu Leu Arg Cys Val Tyr Pro Arg Arg Ser His
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Phe Ser Leu Asp Asp Leu Tyr Val Tyr Trp Gln Ile Val Asp Glu Ala 50 55 60
Lys Thr Val Val Thr Tyr Tyr Leu Pro Ser Ala Asn Glu Ser Ser Thr 65 70 75 80
Ile His Val Ser Asn Ser Tyr Lys Asn Arg Ala His Leu Ser Pro Asp
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                      90
Leu Met Lys Glu Gly Asp Phe Ser Leu His Leu Gln Asn Val Thr Pro 100\,
Gln Asp Thr Gln Glu Phe Lys Cys Leu Val Phe Arg Met Ser Thr Val
Leu Gly Lys Ala Leu Glu Glu Val Val Arg Leu Arg Val Ala Ala Asn
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Glu Arg Thr Phe Thr Cys Met Ser Lys Asn Gly Tyr Pro Glu Pro Asn
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                             170
                                                175
Leu Tyr Trp Ile Asn Arg Thr Asp Asn Thr Leu Ile Asp Glu Thr Leu
       180 185
                                    190
Gln Asn Asn Thr Val Tyr Leu Asn Glu Leu Gly Leu Tyr. Asp Val Val
195 200 205
Ser Thr Leu Arg Ile Pro Trp Thr Pro His Val Asp Val Ile Cys Cys 210 225 220
Val Glu Asn Val Ala Leu His Gln Asn Ile Thr Ser Ile Ser Arg Ala
225 230 235 240
Asp Ser Phe Thr Gly Ser Met Asn Thr Glu Arg Pro Gln Glu Ile His 245 250 255
Arg Glu Ala Thr Lys Val Leu Phe Tyr Ala Leu Ala Ala Leu Leu Ala 260 265 270
Val Val Val Ile Phe Ile Ile Val Leu Tyr Arg Cys Arg Arg Arg
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Thr Val Asn Ala Leu His Pro Gly Val Ala Arg Thr Glu Leu Gly Arg 35 40 45
His Thr Gly Met His Asn Ser Ala Phe Ser Gly Phe Met Leu Gly Pro
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Phe Phe Trp Leu Leu Phe Lys Ser Pro Gln Leu Ala Ala Gln Pro Ser
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Thr Tyr Leu Ala Val Ala Glu Glu Leu Glu Ser Val Ser Gly Lys Tyr
85 90 95
Phe Asp Gly Leu Arg Glu Lys Ala Pro Ser Pro Glu Ala Glu Asp Glu 100 105 110
Glu Val Ala Arg Arg Leu Trp Thr Glu Ser Ala His Leu Val Gly Leu
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Arg Lys Ser Glu Glu Pro Ala Val Arg Lys Lys Glu Ser Ser Leu Arg 35 40
Thr Lys Ile Arg Glu Leu Arg Gln Gln Arg Asp Lys Leu Arg Ala Glu
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Val Lys Gln Trp Gly Ala Arg Val Lys Glu Pro Pro Ala Lys Glu Asp
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Pro Ser Arg Thr Val Ile Ser Glu Gln Glu Val Leu Glu Arg Glu Trp
85 90
Arg Asn Val Asp Ala Ile Leu Glu Ala Tyr Arg Phe Thr Gly Leu Ser 100 105 110
Gly Lys Leu Thr Ser Arg Gly Val Cys Met Cys Ile Ser Thr Ala Phe
  115 120 125
Glu Gly Asn Leu Leu Asp Ser Tyr Phe Val Asp Leu Val Ile Glu Lys
130 135
Pro Leu Arg Ile His His Ser Val Pro Val Phe Ile Pro Leu Glu
                 150
                           155
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Lys Ile Ala Ala Ala His Leu Gln Thr Asp Val Gln Arg Phe Leu Phe
              165
                                 170
                                                 175
Arg Leu Trp Glu Tyr Leu Asn Ala Tyr Ala Gly Arg Lys Tyr Gln Ala
180 185 190
Asp Gln Leu Glu Ser Asp Phe Cys Asp Val Leu Thr Gly Pro Leu Gln 195 200 205
Arg Asn Ala Leu Cys Asn Leu Leu Ser Phe Thr Tyr Lys Val Glu Gln
  210 215 220
Arg Cys Gln Thr Phe Ser Phe Ser Ala Arg Leu Leu Tyr Glu Asp Pro 225 230 240
Thr Ala Ala Leu Pro Thr Asn Val Thr Val Thr Arg Pro Gly Val Glu 245 250 . 255
Ala Ser Ser Pro Pro Trp Glu Glu His Arg Ala Ser His Gln Met Leu 260 265 270
Phe Arg Thr Lys Pro Leu His Lys Val Phe Ala Ser Phe Ser Lys Glu
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Pro Thr Gln Lys Asn Val Ala Gly Ser Lys Arg Val Cys Pro Ser Ser
50 55
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Lys Ile Ile Tyr Tyr Pro Gln Met Ala Pro Val Val Ile Thr Leu Val 65 70 75 80
Ser Asp Gly Ala Arg Cys Leu Leu Ala Arg Gln Ser Ser Phe Pro Lys
85 90 95
Gly Leu Tyr Ser Ala Leu Ala Gly Phe Cys Asp Ile Gly Glu Ser Val
Glu Glu Thr Val His Arg Glu Val Ala Glu Glu Val Gly Leu Glu Val
 115 120 125
Glu Asn Ile Gln Tyr Ser Ala Ser Gln His Trp Pro Phe Pro Asn Ser
130 135 140
Ser Leu Met Ile Ala Cys His Ala Thr Val Lys Pro Gly His Thr Glu
145 150 150 155 156
Ile Gln Val Asn Leu Lys Glu Leu Glu Ala Ala Ala Trp Phe Ser Leu
            165 170 - 175
Asp Glu Val Thr Thr Ala Leu Arg Arg Lys Gly Ser Leu Ala Leu Gln 180 185 190
Pro Ser Glu Ala Ser Pro Leu Leu Pro Pro Lys Leu Ala Ile Ala
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Thr Lys Leu Ser Ala Leu Pro Pro His Gly Ala Pro Gly Val Arg Lys
 50
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                                   60
Val Pro Gly Gln Leu Pro Leu Leu Cys Ser Gly Arg Pro Pro Pro Glu
65 70 75 80
            70
Lys Pro Ala Pro Ile Glu Pro Pro Glu Gly Trp Ser Pro Ala Pro Lys 85 90 95
Glu Pro Gly Cys Arg Gly Arg Gly Arg Glu Val Trp Gly Asp Ile Ala
115 120 125
Asp Ala Ser Ala Trp Asp Pro Val Ala Ser Ile Arg Val Ile Arg Gly 130 140
Cys Trp Ile Leu Tyr Glu Gln Pro Glu Phe Arg Gly Gln Lys Leu Ser
    150 155
Leu Pro Glu Gly Asp Val Glu Leu Arg Ala Leu Ala Cys Ala Trp Ser 165 170 175
Leu Gln Gly Phe Gly Ser Leu Arg Arg Ala Val Gln Asp Tyr Cys Thr 180 185 190
Pro Thr Ile Ser Leu Phe Ser Glu Glu Gly Leu Lys Gly Lys Pro Val 195 200 205
Thr Leu Thr Gly Asp Leu Lys Asp Ser Gln Gly Leu Glu Arg Pro Leu 210 . 220
Gln Val Ala Ser Ala Thr Val Thr Ala Gly Leu Trp Leu Leu Tyr Pro
225 230 235 240
Lys Pro Phe Phe Glu Asp Thr Pro Tyr Ile Leu Glu Pro Gly Glu Tyr
    245 250 255
Pro Thr Leu Glu Ala Trp Gly Thr Ser Gly Pro Ser Val Gly Ser Leu
       260
                         265
                                             270
Lys Pro Met Arg Leu Gly Cys Pro Ser Val Glu Lys Pro Gly Glu Pro
    275
                      280
                                 285
Lys Ala Val Val Tyr Glu Ala Pro Gly Phe Gln Gly Gln Ser Trp Glu 290 295 300
Val Ser Gly Asp Ile Tyr Asn Leu Gln Gln Pro Glu Asp Ser Gln Ser
              310
                                315
Pro Gln Leu Thr Ser Val Gly Ser Leu Arg Ile Leu Gly Gly Cys Trp
                      330 ... 335
             325
Val Gly Tyr Glu Lys Glu Gly Phe Arg Gly His Gln Tyr Leu Leu Glu 340 345 \cdot 350
Glu Gly Glu Tyr Ala Asp Trp Ser His Trp Gly Gly Tyr Asp Glu Leu
355 360 365
Leu Thr Ser Leu Arg Val Ile Arg Thr Asp Phe Gly Asp Pro Ala Val
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Val Leu Phe Glu Asp Met Asp Phe Gln Gly His Arg Val Glu Val Ser
       390 395 400
Ser Ala Leu Pro Asp Val Glu Leu Ala Gln His Gly Pro Ser Thr Gln
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             405
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Ala Ile His Val Leu Ser Gly Val Trp Val Ala Tyr Glu Arg Val Gly 420 425 430
Phe Ser Gly Glu Gln Tyr Ile Leu Glu Lys Gly Val Tyr Arg Asn Cys
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                                         445
Asp Asp Trp Gly Ser Gly Asn Cys Ala Leu Gly Ser Leu Gln Pro Val
 450 455 460
Val Gln Val Gly Glu Ser Asp Leu His Phe Val Thr Lys Ile Gln Leu
                              475
              470
Phe Ser Gly Pro Asn Phe Leu Gly Asp His Ile Ser Phe Glu Asp Asp 485 490 495
Gln Ala Ser Leu Pro Ala Ser Phe His Pro Gln Ser Cys Arg Val His
  500 505 510
Gly Gly Ser Trp Val Leu Phe Glu Asp Lys Asn Phe Glu Ala Asp Gln
               520
                                      525
His Ile Val Ser Glu Gly Glu Phe Pro Thr Leu Thr Asp Met Gly Cys
 530 535 540
Leu Ala Ser Thr Val Leu Gly Ser Leu Arg Lys Val Pro Leu His Phe 545 550 555 560
Ser Glu Pro Ser Leu Ser Leu Phe Gly Leu Glu Cys Phe Glu Gly Lys
           565 570 575
Glu Ile Glu Leu Thr Gly Glu Val Arg Ser Leu Gln Ala Glu Gly Phe
        580 585 590
Asn Asn His Val Leu Ser Val Arg Val Lys Gly Gly Val Trp Val Val 595 600 605
Cys Glu His Ser Asp Phe Arg Gly Arg Gln Trp Leu Val Gly Ser Cys
 610 615
                                    620
Glu Ile Thr Asn Trp Leu Thr Tyr Ser Gly Thr Gln Arg Val Gly Ser
    630 635
Leu Tyr Pro Ile Lys Gln Arg Arg Ala Tyr Phe Arg Leu Trp Asn Ala 645 650 655
Ala Leu Gly Gly Phe Leu Ser Val Pro Asp His Val Glu Asp Met Lys 660 665 670
Ala Gly Arg Val Val Val Ser Glu Pro Arg Ala Gly Gly Ser Cys Ile 675 680 685
Trp Tyr Tyr Glu Asp Gly Leu Leu Lys Asn Gln Met Ala Pro Thr Met 690 700
Ser Leu Gln Val Ile Gly Pro Pro Ser Pro Gly Ser Lys Val Val Leu
705 710 715
Trp Ala Glu Ser Arg Leu Pro Arg Gln Thr Trp Ser Ile Asn Glu Leu 725 730 735
Gly His Ile Cys Ser Gln Met Phe Glu Gly Gln Ile Leu Asp Val Lys 740 745 750 _
Gly Gly Arg Gly Tyr Asp Arg Asp His Val Val Leu Trp Glu Pro Thr
  755 760 765
Lys Asp Arg Leu Ser Gln Ile Trp Thr Val His Val Leu
                    775
                                780
<210> 669
<211> 70
<212> PRT
<213> Mouse
<400> 669
Met Tyr Met Thr Met Arg Gly Lys Glu Pro Trp Gln Thr Ala Lys Leu
          5
                          10
Gln Leu Gly Glu Leu Asn Arg Thr Ala Val Phe Thr Cys Arg Pro Ala
          20
                            25,
```

```
Arg Val Lys Glu Gly Asp Ile Leu Tyr Ile His Ser Leu Gln Thr Val
  35
                 40
                                       45
Gly Ser Asn His Lys Pro Val Ala Ala Glu His Thr Tyr Trp Ala Trp
50 55 .
Pro Glu Glu Thr Asp Val
<210> 670
<211> 368
<212> PRT
<213> Mouse
<400> 670
Leu Thr Asn Gly Ser Gln Ala Ser Asp Lys Ser Glu Glu Gly Ser Ala
           5
                             10
Asp Thr Ala Asp Pro Gln Glu Asn Pro Leu Gln Pro Val Ser Val Gly 20 25 30
Glu Glu Pro Ser Ile Thr Glu His His Ser Val Gly Glu Gln Ala Trp
                                         45
    35 40
Asp Gly Thr Ser Gln Ser Cys Pro Ser Leu Pro Ala Thr Val Ser Phe 50 60
His Met Asp Ser Thr Asp Leu Glu Pro Gly Gln Gln Thr Ala Met Lys 65 70 75 80
Ser Cys Ser Arg Asp Asp Val Glu Met Val Glu Glu Phe Asp Glu Leu
            85 90 95
Pro Thr Asp Ala Val Arg Arg Ile Arg Arg Glu Leu Val Thr Val Thr 100 105 110
       100 105
Lys His Ser Pro Glu Gln Arg Gln Asp Pro Leu Cys Ile Ser Ile Thr 115 120 125
Val Cys Thr Val Glu Lys Asp Arg Pro Ala Ala Leu Asp Ser Leu Glu
 130 135 140
Glu Pro Leu Pro Gly Met Leu Phe Phe Leu Ser Ser Gly Gln Asp Gln 145 150 155 160
Gln Ala His Pro Gln Leu Arg Glu His Pro Ala Pro Glu Ala Ser Glu
165 170 175
Ala Ser Gln Pro Gln Asp Ala Ala Glu Gly Ser Ser Ala Gly Glu Glu
 180 185 · 190
Lys Asp Ala Ser Val Glu Pro Leu Leu Pro Ala Ala Ser Pro Gly Gly
                        200
      195
Ser Thr Ser Gln Val Leu Glu Ala Ala Thr Cys Lys Gln Val Ser 210 225
Gln Asp Phe Leu Glu Thr Arg Phe Lys Ile Gln Gln Leu Leu Glu Pro 225 230 235 240
Gln Gln Tyr Met Ala Cys Leu Pro His His Ile Ile Val Lys Ile Phe
                             250
          245
Arg Leu Leu Pro Thr Leu Ser Leu Ala Ile Leu Lys Cys Thr Cys Arg
        260 265 -·270
Tyr Phe Lys Ser Ile Ile Glu Tyr Tyr Asn Ile Arg Pro Ala Asp Ser 275 280 285
Arg Trp Val Arg Asp Pro Arg Tyr Arg Glu Asp Pro Cys Lys Gln Cys
 290
                  295
                                    300
Lys Lys Lys Tyr Val Lys Gly Asp Val Ser Leu Cys Arg Trp His Pro
            310 315
Lys Pro Tyr Cys Gln Ala Leu Pro Tyr Gly Pro Gly Tyr Trp Met Cys
· 325 330 335
Cys Pro Pro Val Ser Glu Gly Leu Phe Cys Cys Lys Leu Gly Leu His
                            345
```

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Asp Asn His Trp Leu Pro Ala Cys His Ser Phe Asn Pro Gly Asn Pro
355 360
<210> 671
<211> 293
<212> PRT
<213> Mouse
<400> 671
Thr His Phe Ile His Thr Leu Thr Arg Leu Gln Met Glu Gln Gly Ala
1 5 10 15
Glu Ser Leu Gly Asp Leu Glu Ser Pro Val Glu Asp Thr Pro Val Glu
   20
                 25
                                   30
Gln Ala Ala Leu Ser Pro Phe Pro Pro Ser Lys Pro Pro Val Ser Ser
 35 . 40 45
Glu Leu Gly Asp Ser Ser Cys Ser Ser Asp Met Thr Asp Ser Ser Thr 50 60
Thr Leu Ser Ser Gly Ser Ser Glu Pro Pro Asn His Pro Ala His Pro
65 70 75
Ser Leu Pro Gly Pro Ser Phe Arg Ser Gly Val Asp Glu Asp Ser Leu \,{}^{\circ}85 \, 90 \, 95
Glu Gln Ile Leu Asn Phe Ser Asp Ser Asp Leu Gly Ile Glu Glu
                           105
Glu Glu Glu Gly Gly Val Gly Asn Ser Asp Asn Leu Ser Cys Phe
 115 120 125
His Leu Ala Asp Ile Phe Gly Thr Gly Asp Pro Gly Ser Leu Ala Ser
130 135 140
Trp Thr His Ser Gln Ser Gly Ser Ser Leu Ala Ser Gly Ile Leu Asp 145 150 155 160
Glu Asn Ala Asn Leu Asp Ala Ser Cys Phe Leu Asn Ser Gly Leu Gly
  165
                            170 175
Gly Leu Arg Glu Gly Ser Leu Pro Gly Ser Ser Gly Ser Pro Glu Gly 180 185 190
Asp Ala Val Gln Ser Ser Ser Trp Asp Leu Ser Leu Ser Ser Cys Asp
195 200 205
Ser Phe Glu Leu Leu Gln Ala Leu Pro Asp Tyr Ser Leu Gly Pro His
210 215 220
Tyr Thr Ser Arg Arg Val Ser Gly Ser Pro Asp Ser Leu Glu Thr Phe 225 230 235 240
His Pro Leu Pro Ser Phe Ser Pro Pro Arg Asp Ala Ser Thr Cys Phe 245 250 255
Leu Glu Ser Leu Val Gly Leu Ser Glu Pro Val Thr Glu Val Leu Ala 260 265 270
Pro Leu Leu Glu Ser Gln Phe Glu Asp Ala Ala Leu Ala Pro Leu Leu
  275
                 280
Glu Pro Val Pro Val
 290
<210> 672
<211> 904
<212> PRT
<213> Mouse
<400> 672
Met Glu Val Asn Cys Leu Thr Leu Lys Asp Leu Ile Ser Pro Arg Gln
           5 10 15.
Thr Arg Leu Asp Phe Ala Ile Glu Asp Ala Glu Asn Ala Gln Lys Glu
```

			20					25					30		
Asn	Ile	Phe 35		Asp	Arg	Ser	Arg 40		Thr	Pro	Lys	Thr 45		Met	Lys
Asn	Glu 50	Pro	Ile	Asp	Leu	Ser 55	Lys	Gln	Arg	Ile	Phe 60	Thr	Pro	Asp	Arg
Asn 65	Pro	Ile	Thr	Pro	Val 70	Lys	Pro	Val	ąsĄ	Arg 75	Gln	Pro	Gln	Val	Glu 80
Pro	Trp	Thr	Pro	Thr 85	Ala	Asn'	`Leu	Lys	Met 90	Leu	Ile	Ser	Ala	Ala 95	Ser
			100		Arg			105	-				110		
Glu	Asn	Lys 115	Glu	Asp	Ala	Phe	Val 120	Asn	Ser	Leu	Gln	Leu 125	Asp	Val	Ala
	130				Asp	135					140				
145					Leu 150					155					160
				165	Thr				170				_	175	
			180		Val			185					190		
		195			His		200					205			
	210				His	215		•			220	•			
225					Gln 230					235					240
				245	Leu				250					255	
_	_		260	_	Pro			265				•	270		
	_	275			Ser		280			_		285	_		
_	290				Lys	295					300				
305					Asp 310					315					320
				325	His				330					335	
			340		Val Arg			345					350		
		355			Ser	_	360	_				365	. –		
	370				Leu	375	-				380				
385					390 Leu					395					400
				405					410					415	
			420		Gln Gly			425					430		
		435			Gln		440	_				445	_		
	450				Ala	455			_		460				
465				* **	470	v uı	110.	, PLO		475	**6	11-CE	D	110	480

```
Phe Ser Val Ala Gln Thr Asp Leu Pro Ala Phe Ser Ala Gln Asn Gly
        500 505 510
Pro Ser Gly Gln Val Gly Val Pro Val Pro Ser Ala Ala Ser Asp Thr
      515
                   520
                                      525
Glu Asn Leu Lys Pro Ala Leu Leu Ala Gly Gln Pro Leu Val Tyr Val
530 535` 540
Pro Ser Thr Gln Leu Phe Met Leu Tyr Gly Ser Val Gln Glu Gly Leu
545 550 555 560
Ser Pro Glu Ser Arg Ser Glu Glu Asp Gly Gly Gly Ser Asp Val Pro 565 570 575
Ala Asp Leu Ser Val Thr Pro Ser Ala Gln Lys Arg Leu Cys Glu Glu 580 585 590
Arg Asp Pro Gln Glu Glu Glu Asp Glu Pro Ala Met Lys Arg Gln Ser 595 600 605
    595 600
Gln Glu Phe Glu Asp Ser Pro Leu Ser Leu Val Met Pro Lys Lys Pro
 610 615
                                  620
Ser Ser Ser Thr Asp Leu Ala Cys Pro Val Thr Met Gly Asn Gly Ser
   630 635
Ser Pro Pro Leu Glu Aşp Ala Cys Val Lys Gly Gln Leu Pro Ala Ala 645 655
Glu Glu Val Thr Gly Lys Ala Ala Pro Asn Cys Tyr Val Ala Ser Glu
               665
         660
                                           670
Cys Gly Asn Pro Ala Arg Asn Pro Asp Thr Glu Lys Pro Ser Asn Glu
 675 680 685
As Glu Ile Thr Lys Asp Pro Ser Leu Met Gln Tyr Leu Tyr Val Gln 690 \, 700 \,
Ser Pro Ala Gly Leu Asn Gly Phe Asn Met Val Leu Pro Gly Thr Gln
705 710 715
Thr Pro His Thr Val Ala Pro Ser Pro Ala Gln Leu Pro Ser Phe Gly
     725 730 735
Val Pro Cys Met Phe Leu Gln Ser Pro Gly Leu Gly Pro Phe Pro Val 740 745 750
Leu Tyr Ser Pro Ala Ile Pro Gly Pro Ile Ser Ser Ala Pro Gly Thr
    755 760 765
His Pro Asn Pro Gly Pro Met Asn Phe Gly Leu Ser Thr Leu Ala Ser 770 775 780
Ala Ser His Leu Leu Ile Ser Pro Ala Ala Met Val Asn Pro Lys Pro 785 790 790 795 795
Ser Thr Leu Pro Cys Thr Asp Pro Gln Leu Arg Cys Gln Pro Ser Leu
           805 810
Asn Leu Asn Pro Val Met Pro Gly Ser His Gly Val Ile His Pro Glu
820 825 830
Ser Pro Cys Tyr Val Arg His Pro Val Ser Met Val Lys Ala Glu Gln 835 . 840 . 845 .
Ser Pro Ala Pro Ala Thr Pro Lys Ser Ile Gln Arg Arg His Arg Glu 850 855
Thr Phe Phe Lys Thr Pro Gly Ser Leu Gly Asp Pro Val Phe Arg Arg
              870 875
Lys Glu Arg Asn Gln Ser Arg Asn Thr Ser Ser Ala Gln Arg Arg Leu
          885
                            890
Glu Ile Ser Ser Ser Gly Pro Asp
         900
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<213> Mouse
<400> 673
Lys Arg Arg Lys Arg Lys Arg Ser Glu Gly Leu Ser Gln Glu Ala Thr
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                           10 15
Pro Ser Gln Asp Leu Ile Gln His Ser Cys Ser Pro Val Asp His Ser
Glu Pro Glu Ala Arg Thr Glu Leu Gln Lys Lys Lys Lys Lys Lys Arg
35 40 45
                    40
Arg Lys Arg Lys Pro Glu Pro Gln Gln Asp Glu Glu Ser Lys His Pro 50 55
Gly Asp Gln Arg Ser Pro Arg Pro Ser Val Thr Pro Val Pro Ala Leu
              70
Gly Glu Pro Ser Ala Ile Ser Gln Asp Ala Ile Lys Asp Ser Arg Leu 100 \hspace{1cm} 105 \hspace{1cm} 110 \hspace{1cm}
Ala Arg Thr Gln Thr Val Val Asp Asp Trp Asp Glu Glu Phe Asp Arg
 115
                    120
                                     125
Gly Lys Glu Lys Lys Ile Lys Lys Phe Lys Arg Glu Lys Lys Arg Asn
          135 140
Phe Asn Ala Phe Gln Lys Leu Gln Ser Arg Arg Asn Phe Trp Ser Val 145 150 150 155 155
Thr His Pro Ala Lys Val Ala Ser Leu Ser Tyr Arg Arg
          165
                            170
<210> 674
<211> 470
<212> PRT
<213> Mouse
<400> 674
Glu Glu Thr Lys Pro Leu Leu Gly Ser Asp Val Ser Gly Pro Glu Gly 1 5 10 10
Thr Lys Val Met Gly Ala Val Pro Cys Arg Arg Ala Leu Leu Cys
                       25
Asn Gly Met Arg Tyr Lys Leu Leu Gln Glu Gly Asp Ile Gln Val Cys
      35
                     40
Val Ile Arg His Pro Arg Thr Phe Leu Ser Lys Ile Leu Thr Ser Lys
50 55 60
Phe Leu Arg Arg Trp Glu Pro His His Leu Thr Leu Ala Asp Asn Ser 65 70 75 80
Leu Ala Ser Ala Thr Pro Ser Gly Tyr Met Glu Asn Ser Val Ser Tyr
           85
                           90 95
Ser Ala Ile Glu Asp Val Gln Pro Leu Ser Trp Glu Asn Ala Pro Lys
       100 105 - 110
Tyr Cys Leu Gln Leu Thr Ile Pro Gly Gly Thr Val Leu Leu Gln Ala
115 120 125
     115
Ala Asn Ser Tyr Leu Arg Asp Gln Trp Phe His Ser Leu Gln Trp Lys 130 140
165
Ser Pro Leu Gln Asp Asp Ser Ile Asn Gln Ala Pro Leu Glu Ile Val
          180
                          185 .
```

```
Ser Lys Leu Ser Glu Asn Thr Asn Leu Thr Thr Gln Glu His Glu
195 200 205
Asn Ile Ile Val Ala Ile Ala Pro Leu Leu Glu Asn Asn His Pro Pro
                   215
Pro Asp Leu Cys Glu Phe Phe Cys Lys His Cys Arg Glu Arg Pro Arg
            230 235
Ser Met Val Val Ile Glu Val Phe Thr Pro Val Val Gln Arg Ile Leu
245 250 255
Lys His Asn Met Asp Phe Gly Lys Cys Pro Arg Leu Arg Leu Phe Thr 260 265 270
Gln Glu Tyr Ile Leu Ala Leu Asn Glu Leu Asn Ala Gly Met Glu Val
    275 280 285
Val Lys Lys Phe Ile Gln Ser Met His Gly Pro Thr Gly His Cys Pro
290 295 300
His Pro Arg Val Leu Pro Asn Leu Val Ala Val Cys Leu Ala Ala Ile 305
Tyr Ser Cys Tyr Glu Glu Phe Ile Asn Ser Arg Asp Asn Ser Pro Ser
           325 330 335
Leu Lys Glu Ile Arg Asn Gly Cys Gln Gln Pro Cys Asp Arg Lys Pro
       340
                        345
                                  350
Thr Leu Pro Leu Arg Leu Leu His Pro Ser Pro Asp Leu Val Ser Gln 355
Glu Ala Thr Leu Ser Glu Pro Arg Leu Lys Ser Val Val Val Ala Ser
 370 375 380
Ser Glu Val His Val Glu Val Glu Arg Thr Ser Thr Ala Lys Pro Ala
              390
                              395
Leu Thr Ala Ser Thr Gly Asn Asp Ser Glu Pro Asn Leu Ile Asp Cys
           405 410 415
Leu Met Val Ser Pro Ala Cys Gly Thr Met Ser Ile Glu Leu Gly Pro 420 425 430
Gln Ala Gly Arg Thr Leu Gly Cys His Val Glu Ile Leu Lys Leu Leu
  435 440
                              445
Ser Asp Tyr Asp Asp Trp Arg Pro Ser Leu Ala Ser Leu Leu Gln Pro
Ile Pro Phe Pro Lys Glu
             470
465
<210> 675
<211> 319
<212> PRT
<213> Mouse
<400> 675
Phe Ala Arg Thr Leu Pro Trp Ala Ser Val Leu Arg Val Trp Asp Met
                              10
Phe Phe Cys Glu Gly Val Lys Ile Ile Phe Arg Val Ala Leu Val Leu
                 25
Leu Arg His Thr Leu Gly Ser Val Glu Lys Leu Arg Ser Cys Gln Gly
    35 40 45
Met Tyr Glu Thr Met Glu Gln Leu Arg Asn Leu Pro Gln Gln Cys Met
 50
                   55
                                  60
Gln Glu Asp Phe Leu Val His Glu Val Thr Asn Leu Pro Val Thr Glu
             70
                              75 · 80
Ala Trp Ile Glu Arg Glu Asn Ala Ala Gln Leu Lys Lys Trp Arg Glu
        85 90 95
Thr Arg Gly Glu Leu Gln Tyr Arg Pro Ser Arg Arg Leu His Gly Ser
```

100

105

```
Arg Ala Ile His Glu Glu Arg Arg Gln Gln Pro Pro Leu Gly Pro 115 \phantom{0} 120 \phantom{0} 125
Ser Ser Ser Leu Leu Ser Leu Pro Ser Leu Lys Ser Arg Gly Ser Arg
130 135 140
Ala Val Gly Gly Ala Pro Ser Pro Pro Pro Pro Val Arg Arg Ala Ser
145 150 155
Ala Gly Pro Val Pro Gly Ala Val Val Ile Ala Glu Gly Leu His Pro
165 170 175
Ser Leu Pro Ser Pro Thr Gly Asn Ser Thr Pro Leu Gly Thr Ser Lys
180 185 190
        180
Glu Ile Arg Arg Gln Glu Lys Glu Arg Gln Lys Gln Glu Lys Asp Arg
195 200 205
Glu Lys Glu Arg Gln Arg Gln Glu Lys Glu Arg Glu Arg Gln Glu Arg
 210 215
                                 220
Ser Gly Arg Ser Gly Lys Arg Ser Lys Arg Arg Asn Ser Arg Ser Arg 225 230 235
Arg Arg Ser Gly Arg Ser Trp Arg Arg Lys Ala Lys Ala Gly Asn Cys 245 250 255
Pro Cys Val Glu Gly Gln Met Gly Pro Arg His Pro Met Met Val Gly
     260 265 270
Thr Gly Gln Gln Leu Arg Pro Gly Arg Met Leu Thr Phe Asp Leu Trp
 275 280 285
Leu Asp Leu Asp Gly Met Ala Leu Leu Leu Pro Leu Ile Glu Ser Ser 290 295 300
Pro Gly Arg Leu Ser Gln Leu Pro Leu Ala Gly Ser Ser Phe Phe
305 310
                                      315
<210> 676
<211> 94
<212> PRT
<213> Mouse
Met Phe Ser Glu Lys Lys His Phe Leu His Thr Ile Gln Asn Pro Glu 1 \hspace{1.5cm} 5 \hspace{1.5cm} 10 \hspace{1.5cm} 15
Ser Glu Lys Glu Arg Arg Arg Arg Arg Arg Arg Arg Arg Ser Arg Arg 20 \phantom{\bigg|}25\phantom{\bigg|}
Arg Glu Arg Lys Lys Glu Arg Lys Lys Glu Arg Lys Glu Arg Lys
    35
                          40
                                              45
Gln Ala Ser Leu Pro Ser Val Lys Arg Glu Arg Ala Trp His Gly Glu
 50 55
Gln Thr Gln Gly Ser Leu Ser Thr Val Arg Gln Glu Ser Ser Pro Gly 65 70 75 80
His Arg Ala Lys Val Ile Ala Asp Leu Gly Lys Asn Asp Gln
            85
<210> 677
<211> 137
<212> PRT
<213> Mouse
<400> 677
Val Arg Trp Lys Met Arg Arg Ser Leu Arg Ala Gly Arg Arg Arg Gln
          5 10 15
Thr Ala Gly Arg Lys Ser Lys Ser Pro Pro Lys Val Pro Ile Val Ile 20 25 30
Gln Asp Asp Ser Leu Pro Thr Gly Pro Pro Pro Gln Ile Arg Ile Leu
```

```
40
Lys Arg Pro Thr Ser Asn Gly Val Val Ser Ser Pro Asn Ser Thr Ser 50 55 60
Arg Pro Ala Leu Pro Val. Lys Ser Leu Ala Gln Arg Glu Ala Glu Tyr
65 70 75
Ala Glu Ala Arg Arg Ile Leu Gly Ser Ala Ser Pro Glu Glu Glu 85 90 95
Gln Glu Lys Pro Ile Leu Asp`Arg Pro Thr Arg Ile Ser Gln Pro Glu
100 105 110
Asp Ser Arg Gln Pro Ser Asn Val Ile Arg Gln Pro Leu Gly Pro Asp
115 120 125
Gly Ser Gln Gly Phe Lys Gln Arg Arg
 130 135
<210> 678
<211> 380
<212> PRT
<213> Mouse
<400> 678
Glu Thr Thr Ile Thr Thr Asp Ser Arg Asp Tyr Gln Met Ala Lys Gly
                               10 .
            5
Lys Arg Lys Asn Leu Thr Asn Arg Asn Gln Asp His Ser Leu Ser Ser
 20 25 30
Glu Pro Ser Thr Pro Thr Ser Ala Ser Pro Gly Tyr Pro Asp Thr Pro
      35
                      40
                                          45
Glu Lys Gln Asp Ser Asn Leu Lys Ser Tyr Leu Met Met Leu Val Glu
 50 55 60
Asp Ile Lys Lys Gly Phe Asn Asn Ser Leu Lys Glu Val Lys Glu Asn 65 70 75 80
Thr Ala Lys Glu Val Glu Val Leu Lys Glu Ile Gln Glu Asn Thr Thr
            85
                              90 95
Lys Gln Val Met Glu Leu Asn Lys Ile Ile Gln Asp Leu Lys Arg Glu
         100 105 110
Val Glu Thr Lys Lys Thr Gln Asn Glu Thr Thr Leu Glu Ile Glu Thr
115 120 125
Leu Val Lys Lys Ser Gly Thr Ile Asp Val Ser Ile Ser Asn Arg Ile
 130 135
                                     140
Gln Glu Met Glu Glu Arg Ile Ser Gly Ala Glu Asp Ser Ile Glu Asn
145 150 155 160
Ile Gly Thr Thr Thr Lys Glu Asn Ala Lys Arg Lys Lys Ile Leu Thr
165 170 175
Gln Asn Ile Gln Lys Ile Gln Asp Lys Met Arg Arg Pro Asn Leu Trp
180 185 190
Ile Ile Gly Val Asp Glu Asn Glu Asp Ser Gln Leu Lys Gly Pro Ala
195 200 205
Asn Ile Phe Asn Lys Phe Ile Glu Glu Asn Phe Pro Asn Leu Lys Lys 210 215
Glu Met Ser Met Asn Arg Gln Glu Ala Tyr Arg Thr Pro Asn Arg Leu
225 230
                                  235
Asp Gln Lys Arg Asn Ser Ser Leu His Ile Ile Ile Arg Thr Thr Asn 245 250 255
Ala Leu Asn Lys Asp Arg Ile Leu Lys Ala Val Arg Glu Lys Ser Gln 260 265 270
Val Thr Tyr Lys Gly Arg Pro Ile Arg Ile Thr Pro Asp Phe Ser Pro 275 280 285
Glu Thr Met Lys Ala Arg Arg Ser Trp Thr Asp Val Met Gln Thr Leu
```

```
295
                                 300
Arg Glu His Lys Cys Gln Pro Arg Leu Leu Tyr Pro Ala Lys Leu Ser
      310 315
Ile Thr Ile Asp Gly Glu Thr Lys Val Phe His Asp Lys Thr Lys Phe 325 330 335
Thr Gln Tyr Leu Ser Met Asn Pro Gly Leu Gln Arg Ile Ile Lys Gly
340 345 350
Lys His Gln His Lys Asp Gly Asn Tyr Thr Leu Glu Lys Ala Arg Lys
355 360 365
Arg Ser Phe Asn Lys Pro Lys Arg Arg Gln Pro Lys
370
          375
<210> 679
<211> 210
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<213> Mouse
<400> 679
Tyr Gly Thr His Asn His Cys Trp Leu Ser Leu His Arg Gly Phe Ile
                          10
Trp Ser Phe Leu Gly Pro Ala Ala Ile Ile Leu Ile Asn Leu Val
 20
                25
Phe Tyr Phe Leu Ile Ile Trp Ile Leu Arg Ser Lys Leu Ser Ser Leu 35 40 45
35 40
Asn Lys Glu Val Ser Thr Leu Gln Asp Thr Lys Val Met Thr Phe Lys
                55
                               60
Ala Ile Val Gln Leu Phe Val Leu Gly Cys Ser Trp Gly Ile Gly Leu
   70
Phe Ile Phe Ile Glu Val Gly Lys Thr Val Arg Leu Ile Val Ala Tyr
          Leu Phe Thr Ile Ile Asn Val Leu Gln Gly Val Leu Ile Phe Met Val
  100 105 110
His Cys Leu Leu Asn Arg Gln Val Arg Met Glu Tyr Lys Lys Trp Phe
 115 120 125
His Arg Leu Arg Lys Glu Val Glu Ser Glu Ser Thr Glu Val Ser His
130 135 140
Ser Thr Thr His Thr Lys Met Gly Leu Ser Leu Asn Leu Glu Asn Phe 145 150 160
Cys Pro Thr Gly Asn Leu His Asp Pro Ser Asp Ser Ile Leu Pro Ser
    165 170 175
Thr Glu Val Ala Gly Val Tyr Leu Ser Thr Pro Arg Ser His Met Gly
       180 185 190
Ala Glu Asp Val Asn Ser Gly Thr His Ala Tyr Trp Ser Arg Thr Ile
195 200 205
Ser Asp
 210
<210> 680
<211> 373
<212> PRT
<213> Mouse
<400> 680
Met Lys Glu Tyr Val Met Leu Leu Leu Leu Ala Val Cys Ser Ala Lys
               10 15
1 5
Pro Phe Phe Ser Pro Ser His Thr Ala Leu Lys Asn Met Met Leu Lys
         20
                        25,
```

```
35 40 45
Leu Phe Pro Thr Lys Glu Pro Val Asn Pro Phe Phe Pro Phe Asp Leu
 50 55
Phe Pro Thr Cys Pro Phe Gly Cys Gln Cys Tyr Ser Arg Val Val His
                            75
     70
Cys Ser Asp Leu Gly Leu Thr Ser Val Pro Asn Asn Ile Pro Phe Asp
85 90 95
Thr Arg Met Val Asp Leu Gln Asn Asn Lys Ile Lys Glu Ile Lys Glu 100 105 110
Asn Asp Phe Lys Gly Leu Thr Ser Leu Tyr Ala Leu Ile Leu Asn Asn 115 120 125
Asn Lys Leu Thr Lys Ile His Pro Lys Thr Phe Leu Thr Thr Lys Lys
130 135 140
Asn Leu Pro Lys Ser Leu Ala Glu Leu Arg Ile His Asp Asn Lys Val
 165 170 175
Lys Lys Ile Gln Lys Asp Thr Phe Lys Gly Met Asn Ala Leu His Val
180 185 190
Ala Phe Glu Gly Val Thr Val Phe His Ile Arg Ile Ala Glu Ala Lys
210 215 220
Leu Thr Ser Ile Pro Lys Gly Leu Pro Pro Thr Leu Leu Glu Leu His 225 230 235 240
Leu Asp Phe Asn Lys Ile Ser Thr Val Glu Leu Glu Asp Leu Lys Arg 245 250 255
Tyr Arg Glu Leu Gln Arg Leu Gly Leu Gly Asn Asn Arg Ile Thr Asp
 260 265 270
Ile Glu Asn Gly Thr Phe Ala Asn Ile Pro Arg Val Arg Glu Ile His 275 280 280 285
Leu Glu His Asn Lys Leu Lys Lys Ile Pro Ser Gly Leu Gln Glu Leu 290 295 300
Lys Tyr Leu Gln Ile Ile Phe Leu His Tyr Asn Ser Ile Ala Lys Val
305 310 315 320
Tyr Ser Ala Ile Ser Leu Phe Asn Asn Pro Met Lys Tyr Trp Glu Ile
  340 345
                                    350
Gln Pro Ala Thr Phe Arg Cys Val Leu Gly Arg Met Ser Val Gln Leu 355 360 365
Gly Asn Val Gly Lys
370
<210> 681
<211> 466
<212> PRT
<213> Mouse
<400> 681
Met Trp Gly Cys Trp Leu Gly Leu Leu Leu Leu Leu Ala Gly Gln
           5 10 15
Ala Ala Leu Glu Ala Arg Arg Ser Arg Trp Arg Arg Glu Leu Ala Pro
 20 25 30
Gly Leu His Leu Arg Gly Ile Arg Asp Ala Gly Gly Arg Tyr Cys Gln
                   40 ,
     35
```

```
Glu Gln Asp Met Cys Cys Arg Gly Arg Ala Asp Glu Cys Ala Leu Pro
                                 60
Tyr Leu Gly Ala Thr Cys Tyr Cys Asp Leu Phe Cys Asn Arg Thr Val 65 70 80
Ser Asp Cys Cys Pro Asp Phe Trp Asp Phe Cys Leu Gly Ile Pro Pro 85
              85
                                  90
Pro Phe Pro Val Gln Gly Cys Met His Gly Gly Arg Ile Tyr Pro
100 105 110
Val Phe Gly Thr Tyr Trp Asp Asn Cys Asn Arg Cys Thr Cys His Glu
115 120 125
Gly Gly His Trp Glu Cys Asp Gln Glu Pro Cys Leu Val Asp Pro Asp
130 135 140
Met Ile Lys Ala Ile Asn Arg Gly Asn Tyr Gly Trp Gln Ala Gly Asn 145 150 155 160
His Ser Ala Phe Trp Gly Met Thr Leu Asp Glu Gly Ile Arg Tyr Arg 165 170 175
Leu Gly Thr Ile Arg Pro Ser Ser Thr Val Met Asn Met Asn Glu Ile
        180 185 190
Tyr Thr Val Leu Gly Gln Gly Glu Val Leu Pro Thr Ala Phe Glu Ala
    195 200
                                    205
Ser Glu Lys Trp Pro Asn Leu Ile His Glu Pro Leu Asp Gln Gly Asn 210 215 220
Cys Ala Gly Ser Trp Ala Phe Ser Thr Ala Ala Val Ala Ser Asp Arg 225 230 235 240
Val Ser Ile His Ser Leu Gly His Met Thr Pro Ile Leu Ser Pro Gln
              245
                                250
Asn Leu Leu Ser Cys Asp Thr His His Gln Gln Gly Cys Arg Gly Gly 260 265 270
Arg Leu Asp Gly Ala Trp Trp Phe Leu Arg Arg Arg Gly Val Val Ser 275 280 285
Asp Asn Cys Tyr Pro Phe Ser Gly Arg Glu Gln Asn Glu Ala Ser Pro
 290 295
                                        300
Thr Pro Arg Cys Met Met His Ser Arg Ala Met Gly Arg Gly Lys Arg
   310 315
Gln Ala Thr Ser Arg Cys Pro Asn Gly Gln Val Asp Ser Asn Asp Ile . 325 330 335
Tyr Gln Val Thr Pro Ala Tyr Arg Leu Gly Ser Asp Glu Lys Glu Ile 340 350 .
Met Lys Glu Leu Met Glu As<br/>n Gly Pro Val Gl<br/>n Ala Leu Met Glu Val 355 360 365
His Glu Asp Phe Phe Leu Tyr Gln Arg Gly Ile Tyr Ser His Thr Pro 370 375 380 ...
Val Ser Gln Gly Arg Pro Glu Gln Tyr Arg Arg His Gly Thr His Ser
               390
                                      395
Val Lys Ile Thr Gly Trp Gly Glu Glu Thr Leu Pro Asp Gly Arg Thr 405 . 410 . 415
Ile Lys Tyr Trp Thr Ala Ala Asn Ser Trp Gly Pro Trp Trp Gly Glu 420 425 430
Arg Gly His Phe Arg Ile Val Arg Gly Thr Asn Glu Cys Asp Ile Glu
 435 440 445
Thr Phe Val Leu Gly Val Trp Gly Arg Val Gly Met Glu Asp Met Gly
                     455
450
                                   460
His His
465
```

<210> 682 <211> 210

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<400> 682
Met Arg Leu Arg Leu Leu Ala Leu Ala Ala Val Leu Leu Gly Pro
            5
                           10
Ala Pro Glu Val Cys Gly Ala Leu Asn Val Thr Val Ser Pro Gly Pro
      20
                        25
Val Val Asp Tyr Leu Glu Gly Glu Asn Ala Thr Leu Leu Cys His Val
     35
                      40
                                       45
Ser Gln Lys Arg Arg Lys Asp Ser Leu Leu Ala Val Arg Trp Phe Phe
                  55
                                 60
Ala Pro Asp Gly Ser Gln Glu Ala Leu Met Val Lys Met Thr Lys Leu
             70
Arg Ile Ile Gln Tyr Tyr Gly Asn Phe Ser Arg Thr Ala Asn Gln Gln 85 90 95
Arg Leu Arg Leu Leu Glu Glu Arg Arg Gly Val Leu Tyr Arg Leu Ser
   100 105
                                          110
Val Leu Thr Leu Arg Pro Thr Asp Gln Gly Gln Tyr Val Cys Lys Val
     115
                     1.20
                                      125
Gln Glu Ile Ser Lys His Arg Asn Lys Trp Thr Ala Trp Ser Asn Gly
130 135
                                 140
Ser Ser Phe Glu Lys Lys Lys Val Thr Trp Ala Phe Phe Glu Asp Leu
165 170 175
Tyr Val Tyr Ala Val Leu Val Cys Cys Val Gly Ile Leu Ser Val Leu
                              _
190
        180 185
Leu Phe Thr Leu Val Ile Ala Cys Ser Leu Cys Phe Thr Arg Gly Asn
 195
                      200
                                       205
Gln Glu
210
<210> 683
<211> 255
<212> PRT
<213> Mouse
<400> 683
Met Asp Phe Trp Leu Trp Leu Leu Tyr Phe Leu Pro Val Ser Gly Ala
            5
                           10
Leu Arg Val Leu Pro Glu Val Gln Leu Asn Val Glu Trp Gly Gly Ser
       20 25
                                        30
Ile Ile Ile Glu Cys Pro Leu Pro Gln Leu His Val Arg Met Tyr Leu
   35
                     40
                                       45
Cys Arg Gln Met Ala Lys Pro Gly Ile Cys Ser Thr Val Val Ser Asn.
                  55
                           60 ...
Thr Phe Val Lys Lys Glu Tyr Glu Arg Arg Val Thr Leu Thr Pro Cys 70 75 80
Leu Asp Lys Lys Leu Phe Leu Val Glu Met Thr Gln Leu Thr Glu Asn
            85
                          90 95
Asp Asp Gly Ile Tyr Ala Cys Gly Val Gly Met Lys Thr Asp Lys Gly
                 105 . 110
        100
Lys Thr Gln Lys Ile Thr Leu Asn Val His Asn Glu Tyr Pro Glu Pro
    115
                    120 125
Phe Trp Glu Asp Glu Trp Thr Ser Glu Arg Pro Arg Trp Leu His Arg
                                 140
                   135
```

```
Phe Leu Gln His Gln Met Pro Trp Leu His Gly Ser Glu His Pro Ser 145 150 155 160
Ser Ser Gly Val Ile Ala Lys Val Thr Thr Pro Ala Ser Lys Thr Glu
           165 170
                                            175
Ala Pro Pro Val His Gln Pro Ser Ser Ile Thr Ser Val Thr Gln His
       180 185 . 190
Pro Arg Val Tyr Arg Ala Phe Ser Val Ser Ala Thr Lys Ser Pro Ala
195 200 205
Leu Leu Pro Ala Thr Thr Ala Ser Lys Thr Ser Thr Gln Gln Ala Ile
210 215 220
Arg Pro Leu Glu Ala Ser Tyr Ser His His Thr Arg Leu His Glu Gln
              230 235
Arg Thr Arg His His Gly Pro His Tyr Gly Arg Glu Asp Arg Gly
                 250
<210> 684
<211> 228
<212> PRT
<213> Mouse
<400> 684
Met Lys Ala Leu Arg Ala Val Leu Leu Leu Leu Leu Ser Gly Gln
1 5 10 15
Pro Gly Ser Gly Trp Ala Gln Glu Asp Gly Asp Ala Asp Pro Glu Pro
      20
                        25
Thr Asn Met Ile Pro Gly Ser Arg Asp Arg Ala Pro Leu Gln Cys Tyr 50 55
Phe Cys Gln Val Leu His Ser Gly Glu Ser Cys Asn Gln Thr Gln Ser 65 70 75 80 \cdot
Cys Ser Ser Ser Lys Pro Phe Cys Ile Thr Leu Val Ser His Ser Gly
            85 90
Thr Asp Lys Gly Tyr Leu Thr Thr Tyr Ser Met Trp Cys Thr Asp Thr 100 $105\ 
Cys Gln Pro Ile Ile Lys Thr Val Gly Gly Thr Gln Met Thr Gln Thr 115 120 125
Cys Cys Gln Ser Thr Leu Cys Asn Ile Pro Pro Trp Gln Asn Pro Gln
130 135 140
Thr Arg His Pro Gln Gly Gly Lys Phe Ser His Pro Gln Val Val Lys 165 170 175
Ala Ala His Pro Gln Ser Asp Gly Ala Asn Leu Pro Lys Ser Gly Lys
 180 185 190
Ala Asn Gln Pro Gln Gly Ser Gly Ala Gly Tyr Pro Ser Gly Trp Thr.
195 200 205.
Lys Phe Gly Asn Ile Ala Leu Leu Ser Phe Phe Thr Cys Leu Trp
 210
                  215
Ala Ser Gly Ala
225
<210> 685
<211> 242
<212> PRT
<213> Mouse
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Met Ala Ser Gly Trp Phe Tyr Leu Ser Cys Met Val Leu Gly Ser Leu
                            10
Gly Ser Met Cys Ile Leu Phe Thr Ala Tyr Trp Met Gln Tyr Trp Arg
20 25 30
Gly Gly Phe Ala Trp Asp Gly Thr Val Leu Met Phe Asn Trp His Pro
    35
                       40
                                      45
Val Leu Met Val Ala Gly Met Val Val Leu Tyr Gly Ala Ala Ser Leu
50 55 60
Val Tyr Arg Leu Pro Ser Ser Trp Val Gly Pro Arg Leu Pro Trp Lys 65 70 75 80
Val Leu His Ala Ala Leu His Leu Leu Ala Phe Thr Cys Thr Val Val
            85 90 95
Gly Leu Ile Ala Val Phe Arg Phe His Asn His Ser Arg Ile Ala His
       100 105 110
Ala Cys Gln Trp Phe Leu Gly Phe Ala Val Phe Leu Leu Pro Trp Ala
 130 135 140
Ser Gln Trp Leu Arg Ser Leu Leu Lys Pro Leu His Val Phe Gly 145 150 155 160
Ala Cys Ile Leu Ser Leu Ser Ile Thr Ser Val Ile Ser Gly Ile Asn
165 170 175
Glu Lys Leu Phe Phe Val Leu Lys Asn Ala Thr Lys Pro Tyr Ser Ser
 180 185 190
Leu Pro Gly Glu Ala Val Phe Ala Asn Ser Thr Gly Leu Leu Val Val
 195
                200
                                       205
Ala Phe Gly Leu Leu Val Leu Tyr Val Leu Leu Ala Ser Ser Trp Lys 210 215 220
Arg Pro Asp Pro Gly Ala Leu Thr Asp Arg Gln Pro Leu Leu His Asp
225 230
                           235
Arg Glu
<210> 686
<211> 188
<212> PRT
<213> Mouse
<400> 686
Met Arg Leu Pro Leu Pro Leu Leu Leu Leu Phe Gly Cys Arg Ala Ile 1 5 10 10 . 15
Leu Gly Ser Ala Gly Asp Arg Val Ser Leu Ser Ala Ser Ala Pro Thr
                        25
Leu Asp Asp Glu Glu Lys Tyr Ser Ala His Met Pro Ala His Leu Arg
    3.5
                  40
Cys Asp Ala Cys Arg Ala Val Ala Phe Gln Met Gly Gln Arg Leu Ala 50 55 60
Lys Ala Glu Ala Lys Ser His Thr Pro Asp Ala Ser Gly Leu Gln Glu
               70 75 80
Leu Ser Glu Ser Thr Tyr Thr Asp Val Leu Asp Gln Thr Cys Ser Gln
             85
                           90
Asn Trp Gln Ser Tyr Gly Val His Glu Val Asn Gln Met Lys Arg Leu
        1.00
                105 110
Thr Gly Pro Gly Leu Ser Lys Gly Pro Glu Pro Arg Ile Ser Val Met
115 120 125
```

Ile Ser Gly Gly Pro Trp Pro Asn Arg Leu Ser Lys Thr Cys Phe His

```
130
                  135
                                 140
Tyr Leu Gly Glu Phe Gly Glu Asp Gln Ile Tyr Glu Ala Tyr Arg Gln
        150 155
Gly Gln Ala Asn Leu Glu Ala Leu Leu Cys Gly Gly Thr His Gly Pro
165 170 175
Cys Ser Gln Glu Ile Leu Ala Gln Arg Glu Glu Leu
 180 185
<210> 687
<211> 247
<212> PRT
<213> Mouse
<400> 687
Met Ile Pro Gln Val Val Thr Ser Glu Thr Val Thr Val Ile Ser Pro 1 \  \  \,  5
Asn Gly Ile Ser Phe Pro Gln Thr Asp Lys Pro Gln Pro Ser His Gln
      20 25
                           30
Ser Gln Asp Arg Leu Lys Lys His Leu Lys Ala Glu Ile Lys Val Met
                  40
   35
                                  45
Ala Ala Ile Gln Ile Met Cys Ala Val Met Val Leu Ser Leu Gly Ile
50 55
                         60 .
Ile Leu Ala Ser Val Pro Ser Asn Leu His Phe Thr Ser Val Phe Ser 65 70 75 75 80
Ile Leu Leu Glu Ser Gly Tyr Pro Phe Val Gly Ala Leu Phe Phe Ala 85 90 95
Ile Ser Gly Ile Leu Ser Ile Val Thr Glu Lys Lys Met Thr Lys Pro
       100 105 110
Leu Val His Ser Ser Leu Ala Leu Ser Ile Leu Ser Val Leu Ser Ala
115 120 125
Leu Thr Gly Ile Ala Ile Leu Ser Val Ser Leu Ala Ala Leu Glu Pro
130 135 140
Ala Leu Gln Gln Cys Lys Leu Ala Phe Thr Gln Leu Asp Thr Thr Gln
145 150 155 160
Asp Ala Tyr His Phe Phe Ser Pro Glu Pro Leu Asn Ser Cys Phe Val
         165 170
                                         175
Ala Lys Ala Ala Leu Thr Gly Val Phe Ser Leu Met Leu Ile Ser Ser
180 185 190
Val Leu Glu Leu Gly Leu Ala Val Leu Thr Ala Thr Leu Trp Trp Lys
195 200 205
Gln Ser Ser Ala Phe Ser Gly Asn Val Ile Phe Leu Ser Gln Asn
210 215 220
Ser Lys Asn Lys Ser Ser Val Ser Ser Glu Ser Leu Cys Asn Pro Thr
225 230 235
Tyr Glu Asn Ile Leu Thr Ser
            245
<210> 688
<211> 121
<212> PRT
<213> Mouse
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Tyr Gln Arg Arg Ser Lys Thr Leu Glu Glu Leu Ala Asn Asp Ile Lys
                10 15
1
            5
Glu Asp Ala Ile Ala Pro Arg Thr Leu Pro Trp Thr Lys Gly Ser Asp
                      25,
         20
```

```
Thr Ile Ser Lys Asn Gly Thr Leu Ser Ser Val Thr Ser Ala Arg Ala
 35 40 45
Leu Arg Pro Pro Lys Ala Ala Pro Pro Arg Pro Gly Thr Phe Thr Pro
 50
         55
Thr Pro Ser Val Ser Ser Gln Ala Leu Ser Ser Pro Arg Leu Pro Arg
65 70 75
Val Asp Glu Pro Pro Pro Gln Ala Val Ser Leu Thr Pro Gly Gly Val
85 90 95
Ser Ser Ser Ala Leu Ser Arg Met Gly Ala Val Pro Val Met Val Pro 100 100 105 110
Ala Gln Ser Gln Ala Gly Ser Leu Val
              120
<210> 689
<211> 255
<212> PRT
<213> Mouse
<400> 689
Pro Ala Phe Ser Ser Ala Ala Met Ser Trp Ser Pro Ile Leu Pro Phe
1 5 10 15
Leu Ser Leu Leu Leu Leu Phe Pro Leu Glu Val Pro Arg Ala Ala
 20
                          25
Thr Ala Ser Leu Ser Gln Ala Ser Ser Glu Gly Thr Thr Thr Cys Lys
  35 40
                                      45
Val His Asp Val Cys Leu Leu Gly Pro Arg Pro Leu Pro Pro Ser Pro
50 55 60
Pro Val Arg Val Ser Leu Tyr Tyr Glu Ser Leu Cys Gly Ala Cys Arg 65 70 75 80
Tyr Phe Leu Val Arg Asp Leu Phe Pro Thr Trp Leu Met Val Met Glu
           85 90 · 95
Ile Met Asn Ile Thr Leu Val Pro Tyr Gly Asn Ala Gln Glu Arg Asn 100 105 110
Val Ser Gly Thr Trp Glu Phe Thr Cys Gln His Gly Glu Leu Glu Cys
115 120 125
Arg Leu Asn Met Val Glu Ala Cys Leu Leu Asp Lys Leu Glu Lys Glu
 130 135 140
Ala Ala Phe Leu Thr Ile Val Cys Met Glu Glu Met Asp Asp Met Glu
                        155
145 150
Lys Lys Leu Gly Pro Cys Leu Gln Val Tyr Ala Pro Glu Val Ser Pro
165 170 175
Glu Ser Ile Met Glu Cys Ala Thr Gly Lys Arg Gly Thr Gln Leu Met $180$
His Glu Asn Ala Gln Leu Thr Asp Ala Leu His Pro Pro His Glu Tyr
                    200
      195
Val Pro Trp Val Leu Val Asn Glu Lys Pro Leu Lys Asp Pro Ser Glu 210 215 220
Leu Leu Ser Ile Val Cys Gln Leu Asp Gln Gly Thr Glu Lys Pro Asp
225 230 235 235
Ile Cys Ser Ser Ile Ala Asp Ser Pro Arg Lys Val Cys Tyr Lys
                 250 255
<210> 690
<211> 255
<212> PRT
<213> Mouse
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<400> 690
Met Val Trp Thr Gln Asp Arg Leu His Asp Arg Gln Arg Val Val His
            5
                                 10
Trp Asp Leu Ser Gly Asp Pro Gly Ser Gln Arg Arg Arg Leu Val Asp
 20 25 30
Met Tyr Ser Ala Gly Glu Gln Arg Val Tyr Glu Pro Arg Asp Arg Asp 35
                       40
       35
                                              4.5
Arg Leu Leu Ser Pro Ser Ala Phe His Asp Gly Asn Phe Ser Leu 50 55
Leu Ile Arg Ala Val Glu Arg Gly Asp Glu Gly Val Tyr Thr Cys Asn 65 70 75 80
Leu His His His Tyr Cys His Leu Asp Glu Ser Leu Ala Val Arg Leu
85 90 95
             85
                                90 95
Glu Val Thr Asp Asp Pro Leu Leu Ser Arg Ala Tyr Trp Asp Gly Glu
100 105 110
Lys Glu Val Leu Val Val Ala His Gly Ala Pro Ala Leu Met Thr Cys
115 120 125
Ile Asn Arg Ala His Val Trp Thr Asp Arg His Leu Glu Glu Ala Gln
 130 . 135
                               140
Gln Val Val His Trp Asp Arg Gln Leu Pro Gly Val Ser His Asp Arg 145 \phantom{\bigg|} 150 \phantom{\bigg|} 155 \phantom{\bigg|} 160
Ala Asp Arg Leu Leu Asp Leu Tyr Ala Ser Gly Glu Arg Arg Ala Tyr
165 170 175
Gly Pro Pro Phe Leu Arg Asp Arg Val Ser Val Asn Thr Asn Ala Phe
     180 185 190
Ala Arg Gly Asp Phe Ser Leu Arg Ile Asp Glu Leu Glu Arg Ala Asp
195 200 205
Glu Gly Ile Tyr Ser Cys His Leu His His His Tyr Cys Gly Leu His 210 215 220
Glu Arg Arg Val Phe His Leu Gln Val Thr Glu Pro Ala Phe Glu Pro
225 230 235
Pro Ala Arg Ala Ser Pro Gly Asn Gly Ser Gly His Ser Ser Ala
 . 245
                                  250 · 255
<210> 691
<211> 255
<212> PRT
<213> Mouse
<400> 691
Met Lys Leu Lys Gln Arg Val Val Leu Leu Ala Ile Leu Leu Val Ile 1 5 5 10 10 15
Phe Ile Phe Thr Lys Val Phe Leu Ile Asp Asn Leu Asp Thr Ser Ala
       2.0
                              25
Ala Asn Arg Glu Asp Gln Arg Ala Phe His Arg Met Met Thr Gly Leu
 35
                    40 45
Arg Val Glu Leu Val Pro Lys Leu Asp His Thr Leu Gln Ser Pro Trp 50 60
Glu Ile Ala Ala Gln Trp Val Val Pro Arg Glu Val Tyr Pro Glu Glu
               70
                                    75
Thr Pro Glu Leu Gly Ala Ile Met His Ala Met Ala Thr Lys Lys Ile
            85 90
Ile Lys Ala Asp Val Gly Tyr Lys Gly Thr Gln Leu Lys Ala Leu Leu 100 105 110

Ile Leu Glu Gly Gly Gln Lys Val Val Phe Lys Pro Lys Arg Tyr Ser 120 125
```

Arg Asp Tyr Val Val Glu Gly Glu Pro Tyr Ala Gly Tyr Asp Arg His

```
130
                       135
                                          140
Asn Ala Glu Val Ala Ala Phe His Leu Asp Arg Ile Leu Gly Phe Arg
        150 155<sup>-</sup>
Arg Ala Pro Leu Val Val Gly Arg Tyr Val Asn Leu Arg Thr Glu Val
165 170 175
Lys Pro Val Ala Thr Glu Gln Leu Leu Ser Thr Phe Leu Thr Val Gly
          180
                            185
                                      190
Asn Asn Thr Cys Phe Tyr Gly Lys Cys Tyr Tyr Cys Arg Glu Thr Glu
195 200 205
Pro Ala Cys Ala Asp Gly Asp Met Met Glu Gly Ser Val Thr Leu Trp 210 215 220
Leu Pro Asp Val Trp Pro Leu Gln Lys His Arg His Pro Trp Gly Arg
225 230 235
Thr Tyr Arg Glu Gly Lys Leu Ala Arg Trp Glu Tyr Asp Glu Ser
<210> 692
<211> 255
<212> PRT
<213> Mouse
<400> 692
Met Gln Thr Met Trp Gly Ser Gly Glu Leu Leu Val Ala Trp Phe Leu
1 5
                                 10
Val Leu Ala Ala Asp Gly Thr Thr Glu His Val Tyr Arg Pro Ser Arg
         20
                             25
                                            30
Arg Val Cys Thr Val Gly Ile Ser Gly Gly Ser Ile Ser Glu Thr Phe 35
Val Gln Arg Val Tyr Gln Pro Tyr Leu Thr Thr Cys Asp Gly His Arg
50 55
Ala Cys Ser Thr Tyr Arg Thr Ile Tyr Arg Thr Ala Tyr Arg Arg Ser 65 70 75 80
Pro Gly Val Thr Pro Ala Arg Pro Arg Tyr Ala Cys Cys Pro Gly Trp 85 90 95
                                90
Lys Arg Thr Ser Gly Leu Pro Gly Ala Cys Gly Ala Ala Ile Cys Gln
100 105 110
Pro Pro Cys Gly Asn Gly Gly Ser Cys Ile Arg Pro Gly His Cys Arg
Cys Pro Val Gly Trp Gln Gly Asp Thr Cys Gln Thr Asp Val Asp Glu
130 135
                               140
Cys Ser Thr Gly Glu Ala Ser Cys Pro Gln Arg Cys Val Asn Thr Val 145 150 155 160
Gly Ser Tyr Trp Cys Gln Gly Trp Glu Gly Gln Ser Pro Ser Ala Asp
165 170 175
Gly Thr Arg Cys Leu Ser Lys Glu Gly Pro Ser Pro Val Ala Pro Asn
180 185 190 .
Pro Thr Ala Gly Val Asp Ser Met Ala Arg Glu Glu Val Tyr Arg Leu 195 . 200 205
Gln Ala Arg Val Asp Val Leu Glu Gln Lys Leu Gln Leu Val Leu Ala
 210 215 220
Pro Leu His Ser Leu Ala Ser Arg Ser Thr Glu His Gly Leu Gln Asp
225 230
                           235
Pro Gly Ser Leu Leu Ala His Ser Phe Gln Gln Leu Asp Arg Ile
              245
                                 250
<210> 693
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367

<211> 255

<212> PRT <213> Mouse <400> 693 Met Arg Leu Thr Val Gly Ala Leu Leu Ala Cys Ala Ala Leu Gly Leu 5 10 1.5 Cys Leu Ala Val Pro Asp Lys Thr Val Lys Trp Cys Ala Val Ser Glu 20 25 30 20 His Glu Asn Thr Lys Cys Ile Ser Phe Arg Asp His Met Lys Thr Val $40 \hspace{1.5cm} 40 \hspace{1.5cm} 45$ 35 Leu Pro Pro Asp Gly Pro Arg Leu Ala Cys Val Lys Lys Thr Ser Tyr 50 55 60 Pro Asp Cys Ile Lys Ala Ile Ser Ala Ser Glu Ala Asp Ala Met Thr 65 70 75 80 Leu Asp Gly Gly Trp Val Tyr Asp Ala Gly Leu Thr Pro Asn Asn Leu 85 90 95 Lys Pro Val Ala Ala Glu Phe Tyr Gly Ser Val Glu His Pro Gln Thr 105 110 100 Tyr Tyr Tyr Ala Val Ala Val Val Lys Lys Gly Thr Asp Phe Gln Leu
115 120 125 115 120 125 Asn Gln Leu Glu Gly Lys Lys Ser Cys His Thr Gly Leu Gly Arg Ser 130 135 140 Ala Gly Trp Val Ile Pro Ile Gly Leu Leu Phe Cys Lys Leu Ser Glu 145 150 150 155 160Pro Arg Ser Pro Leu Glu Lys Ala Val Ser Ser Phe Phe Ser Gly Ser 165 170 175 Cys Val Pro Cys Ala Asp Pro Val Ala Phe Pro Lys Leu Cys Gln Leu 180 \$185\$Cys Pro Gly Cys Gly Cys Ser Ser Thr Gln Pro Phe Phe Gly Tyr Val 195 200 205 Gly Ala Phe Lys Cys Leu Lys Asp Gly Gly Gly Asp Val Ala Phe Val 210 215 220 Lys His Thr Thr Ile Phe Glu Val Leu Pro Glu Lys Ala Asp Arg Asp 230 235 Gln Tyr Glu Leu Leu Cys Leu Asp Asn Thr Arg Lys Pro Val Asp 245 250 <210> 694 <211> 255 <212> PRT <213> Mouse <400> 694 Gly Ala Pro Thr Pro Ala Tyr Val Arg Ser Ala Arg Arg Thr Glu Pro 15 Leu Ala Ser Gly Ala Arg Ser Arg Leu Cys Gln Cys Arg Arg Val Pro 20 25 25 2520 25 Ala Arg Lys Gln Gly Pro Gln Glu Gln Gly Gly Ser Gly Glu Ser Thr 35 40 45 Thr Ser Ser Pro Gln Trp Trp Arg Arg Trp Arg Arg Leu Trp Ser Thr 50 55 Cys Ser Cys Ser Ala Asp Asp Arg His Thr Gly Ser His Thr Asp Leu 70 75 · Lys Glu Glu Thr Pro Ser Trp Thr Gln Ile Ser Val Val Phe Arg Lys 85 90 95 Asp Gly Gln Asp Glu Leu Gln Ala Ala His Lys Ala His Gly Ser Gly 105

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Ser Pro Leu Thr Asn Gln Glu Ile Pro Ser Ser Ser Gly Ser Gly Phe
 115 120 125
Ile Val Ser Glu Asp Gly Leu Ile Val Thr Asn Ala His Val Leu Thr
                     135
                                   1.40
Asn Gln Gln Lys Ile Gln Val Glu Leu Gln Ser Gly Ala Arg Tyr Glu
145 150 155
Ala Thr Val Lys Asp Ile Asp His Lys Leu Asp Leu Ala Leu Ile Lys
165 170 170
Ile Glu Pro Asp Thr Glu Leu Pro Val Leu Leu Gly Arg Ser Ser 180 185 190
Asp Leu Arg Ala Gly Glu Phe Val Val Ala Leu Gly Ser Pro Phe Ser 195 200 205
Leu Gln Asn Thr Val Thr Ala Gly Ile Val Ser Thr Thr Gln Arg Gly
                 215
                                     220
Gly Arg Glu Leu Gly Leu Lys Asn Ser Asp Ile Asp Tyr Ile Gln Thr 225 230 240
Asp Ala Ile Ile Asn His Gly Asn Ser Gly Gly Pro Leu Val Asn
             245
                              250
<210> 695
<211> 174
<212> PRT
<213> Mouse
<400> 695
Met Pro Ala Cys Arg Leu Cys Leu Leu Ala Ala Gly Leu Leu Gly
                               10
Leu Leu Phe Thr Pro Ile Ser Ala Thr Gly Thr Asp Ala Glu Lys
20 25 30
 20
                          25
                                         30
Pro Gly Glu Cys Pro Gln Leu Glu Pro Ile Thr Asp Cys Val Leu Glu
                     40
                                      45
Cys Thr Leu Asp Lys Asp Cys Ala Asp Asn Arg Lys Cys Cys Gln Ala
 50
                  55
                                     60
Gly Cys Ser Ser Val Cys Ser Lys Pro Asn Gly Pro Ser Glu Gly Glu 65 70 75 80
Leu Ser Gly Thr Asp Thr Lys Leu Ser Glu Thr Gly Thr Thr Thr Gln 85 90
Ser Ala Gly Leu Asp His Thr Thr Lys Pro Pro Gly Gly Gln Val Ser
         100
                         105
                                            110
Thr Lys Pro Pro Ala Val Thr Arg Glu Gly Leu Gly Val Arg Glu Lys
                                 125
     115
                     120
Gln Gly Thr Cys Pro Ser Val Asp Ile Pro Lys Leu Gly Leu Cys Glu
130 135 140
Asp Gln Cys Gln Val Asp Ser Gln Cys Ser Gly Asn Met Lys Cys
        150 155 160
Arg Asn Gly Cys Gly Lys Met Ala Cys Thr Thr Pro Lys Phe
                    170
<210> 696
<211> 193
<212> PRT
<213> Mouse
<400> 696
Leu Ala Thr Leu Val Gln Val Ser Arg Ile Arg Ala Tyr Ser Gln Gly
1 5 10 15
Gln Thr Gln Asp Gln Gln Gly Ser Ser Ser Leu Asp Lys Val Ala Val
```

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20
                          25
Pro Arg Glu Gln Thr His Ser Gly Leu Glu Gln Ile Gln Gln Ile Gln 35 40 45
Gln Gln Leu Thr Gln Phe Asn Ala Ser Leu Ala Gly Leu Cys Arg Pro
 50 55
Cys Pro Trp Asp Trp Glu Leu Phe Gln Gly Ser Cys Tyr Leu Phe Ser 65 70 75 80
Arg Thr Leu Gly Ser Trp Glu`Thr Ser Ala Ser Ser Cys Glu Asp Leu 85 90 95
Gly Ala His Leu Val Ile Val Asn Ser Val Ser Glu Gln Arg Phe Met
 100 105 110
Lys Tyr Trp Asn Val Arg Lys Asn Gln Arg Ser Trp Ile Gly Leu Ser
    115
                     120
                                    125
Asp His Ile His Glu Gly Ser Trp Gln Trp Val Asp Gly Ser Ala Leu
130 135 140
Asp Cys Val Glu Leu Phe Met Asp Asp Trp Asn Asp Asn Lys Cys Thr
          165 170 175
Glu Gln Asn Phe Trp Val Cys Glu Gln Pro Ser Ala Pro Cys Pro His
<210> 697
<211> 173
<212> PRT
<213> Mouse
Val Arg Asn Gly Asp Leu Phe Phe Lys Lys Val Gln Val Glu Asp Gly
             5
                            10
                                             15
Ser Val Glu Leu Lys Val Tyr Asn Phe Thr Leu His Gly His His Asp
   35
                    40
                                45
Thr Leu Asn Thr Ala Tyr Thr Thr Leu Val Gly Cys Ile Leu Ser Val
                 55
                                 60
Val Leu Val Leu Ile Tyr Leu Tyr Leu Thr Pro Cys Arg Cys Trp Cys 65 70 75 80
Arg Gly Val Glu Lys Pro Ser Ser His Gln Gly Asp Ser Leu Ser Ser 85 90 95
Ser Met Leu Ser Thr Thr Pro Asn His Asp Pro Met Ala Gly Gly Asp 100 105 110
Lys Asp Asp Gly Phe Asp Arg Arg Val Ala Phe Leu Glu Pro Ala Gly
   115
              120 125
Pro Gly Gln Gly Gln Asn Gly Lys Leu Lys Pro Gly Asn Thr Leu Pro
130 135 140
Val Pro Glu Ala Thr Gly Lys Gly Gln Arg Arg Met Ser Asp Pro Glu
             150 155
Ser Val Ser Ser Val Phe Ser Asp Thr Pro Ile Val Val
          165
                    170
<210> 698
<211> 88
<212> PRT
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<213> Mouse

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<400> 698
Met Glu Glu Ile Thr Cys Ala Phe Leu Leu Leu Leu Ala Gly Leu Pro
              5
                               10
Ala Leu Glu Ala Ser Asp Pro Val Asp Lys Asp Ser Pro Phe Tyr Tyr
          2.0
                          25
                                             30
Asp Trp Glu Ser Leu Gln Leu Gly Gly Leu Ile Phe Gly Gly Leu Leu
      35
                      `40
                                       45
Cys Ile Ala Gly Ile Ala Met Ala Leu Ser Gly Lys Cys Lys Cys Arg
50 55
                   55
                                      60
Arg Thr His Lys Pro Ser Ser Leu Pro Gly Lys Ala Thr Pro Leu Ile
               70
Ile Pro Gly Ser Ala Asn Thr Cys
              85
<210> 699
<211> 155
<212> PRT
<213> Mouse
<400> 699
Met Tyr Ser Glu Gly Ala Pro Phe Trp Thr Gly Ile Val Ala Met Leu
1 5
                                10
Ala Gly Ala Val Ala Phe Leu His Lys Lys Arg Gly Gly Thr Cys Trp
        20
                            25
                                              30
Ala Leu Met Arg Thr Leu Leu Val Leu Ala Ser Phe Cys Thr Ala Val
                      40
                                        45
Ala Ala Ile Val Ile Gly Ser Arg Glu Leu Asn Tyr Tyr Trp Tyr Phe 50 60
                                      60
Leu Gly Asp Asp Val Cys Gln Arg Asp Ser Ser Tyr Gly Trp Ser Thr
               ·70
                                 75
Met Pro Arg Thr Thr Pro Val Pro Glu Glu Ala Asp Arg Ile Ala Leu
           85
                      90
Cys Ile Tyr Tyr Thr Ser Met Leu Lys Thr Leu Leu Met Ser Leu Gln 100 105 110
Ala Met Leu Leu Gly Ile Trp Val Leu Leu Leu Leu Ala Ser Leu Thr
    115
                     120 125
Pro Val Cys Val Tyr Ile Trp Lys Arg Phe Phe Thr Lys Ala Glu Thr
 130
                  135 140
Glu Glu Lys Lys Leu Leu Gly Ala Ala Val Ile
              150
<210> 700
<211> 255
<212> PRT
<213> Mouse
<400> 700
Met Leu Gln His Thr Ser Leu Val Leu Leu Leu Ala Ser Ile Trp Thr
1
              5
                                1.0
Thr Arg His Pro Val Gln Gly Ala Asp Leu Val Gln Asp Leu Ser Ile
                          25
Ser Thr Cys Arg Ile Met Gly Val Ala Leu Val Gly Arg Asn Lys Asn
               40
     35
                                         45
Pro Gln Met Asn Phe Thr Glu Ala Asn Glu Ala Cys Lys Met Leu Gly
 50
                   55
                                      60
Leu Thr Leu Ala Ser Arg Asp Gln Val, Glu Ser Ala Gln Lys Ser Gly
```

```
70
                                 75
Phe Glu Thr Cys Ser Tyr Gly Trp Val Gly Glu Gln Phe Ser Val Ile
                          90 95
           85
Pro Arg Ile Phe Ser Asn Pro Arg Cys Gly Lys Asn Gly Lys Gly Val
                                         110
Leu Ile Trp Asn Ala Pro Ser Ser Gln Lys Phe Lys Ala Tyr Cys His
115
Asn Ser Ser Asp Thr Trp Val Asn Ser Cys Ile Pro Glu Ile Val Thr
 130 135 140
Thr Phe Tyr Pro Val Leu Asp Thr Gln Thr Pro Ala Thr Glu Phe Ser
145 150
                                155 160
Val Ser Ser Ser Ala Tyr Leu Ala Ser Ser Pro Asp Ser Thr Thr Pro
           165
                  170 175
Val Ser Ala Thr Thr Arg Ala Pro Pro Leu Thr Ser Met Ala Arg Lys
                 185 190
       180
Thr Lys Lys Ile Cys Ile Thr Glu Val Tyr Thr Glu Pro Ile Thr Met 195 200 205
Ala Thr Glu Thr Glu Ala Phe Val Ala Ser Gly Ala Ala Phe Lys Asn
 210 215 220
Glu Ala Ala Gly Phe Gly Gly Val Pro Thr Ala Leu Leu Val Leu Ala
225 230
                       235
Leu Leu Phe Phe Gly Ala Ala Ala Val Leu Ala Val Cys Tyr Val
 245
                   250
<210> 701
<211> 91
<212> PRT
<213> Mouse
<400> 701
Met Val Trp Ala Asn Leu Ala Val Phe Val Ile Cys Phe Leu Pro Leu
          5
                          10
His Val Val Leu Thr Val Gln Val Ser Leu Asn Leu Asn Thr Cys Ala
 20
                       25
                                        30
Ala Arg Asp Thr Phe Ser Arg Ala Leu Ser Ile Thr Gly Lys Leu Ser
    35
                    40
                                    45
Asp Thr Asn Cys Cys Leu Asp Ala Ile Cys Tyr Tyr Tyr Met Ala Arg
50 55
Glu Phe Gln Glu Ala Ser Lys Pro Ala Thr Ser Ser Asn Thr Pro His
·65 70
                                75
Lys Ser Gln Asp Ser Gln Ile Leu Ser Leu Thr
            85
<210> 702
<211> 244
<212> PRT
<213> Mouse
<400> 702
Gly Trp Gln Gly Ala Pro Asp Pro Arg Gly Leu Gly Gln Leu Ser Gln
             5
                   10
Pro Tyr Met Gly Glu Met Pro Trp Thr Ile Leu Leu Phe Ala Ser
                      25
                                 . 30
Gly Ser Leu Ala Ile Pro Ala Pro Ser Ile Ser Leu Val Pro Pro Tyr
   35
                   40 45
Pro Ser Ser His Glu Asp Pro Ile Tyr Ile Ser Cys Thr Ala Pro Gly
```

55

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Asp Ile Leu Gly Ala Asn Phe Thr Leu Phe Arg Gly Gly Glu Val Val
    70 - 75
Gln Leu Leu Gln Ala Pro Ser Asp Arg Pro Asp Val Thr Phe Asn Val
Thr Gly Gly Gly Gly Gly Gly Glu Ala Ala Gly Gly Asn Phe
100 105 110
Cys Cys Gln Tyr Gly Val Met Gly Glu His Ser Gln Pro Gln Leu Ser
115 120 125
                                 125
Asp Phe Ser Gln Gln Val Gln Val Ser Phe Pro Val Pro Thr Trp Ile
130 135 140
Leu Ala Leu Ser Leu Ser Leu Ala Gly Ala Val Leu Phe Ser Gly Leu
145 150 155 160
Val Ala Ile Thr Val Leu Val Arg Lys Ala Lys Ala Lys Asn Leu Gln
165 170 175
Lys Gln Arg Glu Arg Glu Ser Cys Trp Ala Gln Ile Asn Phe Thr Asn 180 185 190
Thr Asp Met Ser Phe Asp Asn Ser Leu Phe Ala Ile Ser Thr Lys Met
 195 200 205
Thr Gln Glu Asp Ser Val Ala Thr Leu Asp Ser Gly Pro Arg Lys Arg
 210 215
                              220
Pro Thr Ser Ala Ser Ser Pro Glu Pro Pro Glu Phe Ser Thr Phe
225 . 230
                            235
Arg Ala Cys Gln
<210> 703
<211> 255
<212> PRT
<213> Mouse
<400> 703
Met Ala Gln Leu Ala Arg Ala Thr Arg Ser Pro Leu Ser Trp Leu Leu 1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15
Leu Leu Phe Cys Tyr Ala Leu Arg Lys Ala Gly Gly Asp Ile Arg Val
20 25 30
Leu Val Pro Tyr Asn Ser Thr Gly Val Leu Gly Gly Ser Thr Thr Leu
 35 40 45
His Cys Ser Leu Thr Ser Asn Glu Asn Val Thr Ile Thr Gln Ile Thr 50 55 60
Trp Met Lys Lys Asp Ser Gly Gly Ser His Ala Leu Val Ala Val Phe 65 70 80
His Pro Lys Lys Gly Pro Asn Ile Lys Glu Pro Glu Arg Val Lys Phe 85 90 95
```

| Ser | Ser

```
Val Pro Ser Arg Gln Ala Asp Gly Lys Asn Ile Thr Cys Thr Val Glu 210 215 220
His Glu Ser Leu Gln Glu Leu Asp Gln Leu Leu Val Thr Leu Ser Gln
225 230 235 240
Pro Tyr Pro Pro Glu Asn Val Ser Ile Ser Gly Tyr Asp Gly Asn
           245
                           250
<210> 704
<211> 255
<212> PRT
<213> Mouse
<400> 704
Met Phe Leu Val Gly Ser Leu Val Val Leu Cys Gly Leu Leu Ala His
           5 10 15
Ser Thr Ala Gln Leu Ala Gly Leu Pro Leu Pro Leu Gly Gln Gly Pro
 20
                       25
                                  30
Pro Leu Pro Leu Asn Gln Gly Pro Pro Leu Pro Leu Asn Gln Gly Gln
                      40
35
Leu Leu Pro Leu Ala Gln Gly Leu Pro Leu Ala Val Ser Pro Ala Leu
50 55
                            60
Pro Ser Asn Pro Thr Asp Leu Leu Ala Gly Lys Phe Thr Asp Ala Leu 65 70 75
Ser Gly Gly Leu Leu Ser Gly Gly Leu Leu Gly Ile Leu Glu Asn Ile
           85
                           90 95
Pro Leu Leu Asp Val Ile Lys Ser Gly Gly Gly Asn Ser Asn Gly Leu 100 105 110
Val Gly Gly Leu Leu Gly Lys Leu Thr Ser Ser Val Pro Leu Leu Asn
115 120 125
                     120 125
Asn Ile Leu Asp Ile Lys Ile Thr Asp Pro Gln Leu Leu Glu Leu Gly
 130 135 140
Leu Val Gln Ser Pro Asp Gly His Arg Leu Tyr Val Thr Ile Pro Leu 145 150 155 160
Gly Leu Thr Leu Asn Val Asn Met Pro Val Val Gly Ser Leu Leu Gln
165 170 175
Leu Ala Val Lys Leu Asn Ile Thr Ala Glu Val Leu Ala Val Lys Asp
       180 185 190
Asn Gln Gly Arg Ile His Leu Val Leu Gly Asp Cys Thr His Ser Pro
 195
                     200
                                       205
Gly Ser Leu Lys Ile Ser Leu Leu Asn Gly Val Thr Pro Val Gln Ser
 210 215 220
Phe Leu Asp Asn Leu Thr Gly Ile Leu Thr Lys Val Leu Pro Glu Leu 225 230 240
Ile Gln Gly Lys Val Cys Pro Leu Val Asn Gly Ile Leu Ser Gly
 245 250
                                     255
<210> 705
<211> 255
<212> PRT
<213> Mouse
<400> 705
Met Ala Thr Thr Cys Gln Val Val Gly Leu Leu Leu Ser Leu Leu 1 5
Gly Leu Ala Gly Cys Ile Ala Ala Thr Gly Met Asp Met Trp Ser Thr
         20
                       25 . 30
Gln Asp Leu Tyr Asp Asn Pro Val Thr Ala Val Phe Gln His Glu Gly
```

```
35
                          40
Leu Trp Arg Ser Cys Val Gln Gln Ser Ser Gly Phe Thr Glu Cys Arg 50 60
Pro Tyr Phe Thr Ile Leu Gly Leu Pro Ala Met Leu Gln Ala Val Arg 65 70 75 80
Ala Leu Met Ile Val Gly Ile Val Leu Gly Val Ile Gly Ile Leu Val 85 90 95
Ser Ile Phe Ala Leu Lys Cys`Ile Arg Ile Gly Ser Mét Asp Asp Ser
100 105 110
Ala Lys Ala Lys Met Thr Leu Thr Ser Gly Ile Leu Phe Ile Ile Ser 115 120 125
Gly Ile Cys Ala Ile Ile Gly Val Ser Val Phe Ala Asn Met Leu Val
  130 135 140
Thr Asn Phe Trp Met Ser Thr Ala Asn Met Tyr Ser Gly Met Gly Gly
        150
                           155
Met Gly Gly Met Val Gln Thr Val Gln Thr Arg Tyr Thr Phe Gly Ala
165 170
Ala Leu Phe Val Gly Trp Val Ala Gly Gly Leu Thr Leu Ile Gly Gly 180 185 190
Val Met Met Cys Ile Ala Cys Arg Gly Leu Thr Pro Asp Asp Ser Asn 195 200 205
 195
Phe Lys Ala Val Ser Tyr His Ala Ser Gly Gln Asn Val Ala Tyr Arg
210 215 220
                              220
Pro Gly Gly Phe Lys Ala Ser Thr Gly Phe Gly Ser Asn Thr Arg Asn
225 230 235 240
Lys Lys Ile Tyr Asp Gly Gly Ala Arg Thr Glu Asp Asp Glu Gln
              245
                                 250
<210> 706
<211> 255
<212> PRT
<213> Mouse
<400> 706
Met Gly Arg Phe Ala Ala Ala Leu Val Gly Ser Leu Phe Trp Leu Gly
           5
                                 10
Leu Leu Cys Gly Leu Gly Ser Leu Ala Ser Ala Glu Pro Arg Ala
. 20
                            25
                                           3.0
Pro Pro Asn Arg Ile Ala Ile Val Gly Ala Gly Ile Gly Gly Thr Ser
35
               40
Ser Ala Tyr Tyr Leu Arg Lys Lys Phe Gly Lys Asp Val Lys Ile Asp 50 60
                     55
Val Phe Glu Arg Glu Glu Val Gly Gly Arg Leu Ala Thr Leu Lys Val
              70
                                75
Gln Gly His Asp Tyr Glu Ala Gly Gly Ser Val Ile His Pro Leu Asn
85 90 95
Leu His Met Lys Arg Phe Val Lys Glu Leu Gly Leu Ser Ser Val Pro
100 105
Ala Ser Gly Gly Leu Val Gly Val Tyr Asn Gly Lys Ser Leu Val Phe
    115
                        120 125
Glu Glu Ser Ser Trp Phe Val Ile Asn Val Ile Lys Leu Val Trp Arg
130 135
                              140
Tyr Gly Phe Gln Ser Leu Arg Met His Met Trp Val Glu Asp Leu Leu 145 150 155 160
Asp Lys Phe Met Arg Ile Tyr Arg Tyr Gln Ser His Asp Tyr Ala Phe 165 170 175
```

Ser Ser Val Glu Lys Leu Met His Ala Ile Gly Gly Asp Asp Tyr Val

```
180
                             185
                                              190
Arg Leu Leu Asn Gln Thr Leu Arg Glu Asn Leu Lys Lys Ala Gly Phe 195 200 205
Ser Glu Thr Phe Leu Asn Glu Met Ile Ala Pro Val Met Lys Val Asn
 210 215 220
Tyr Gly Gln Ser Thr Asp Ile Asn Ala Phe Val Gly Ala Val Ser Leu 225 235 240
Thr Ala Ala Asp Ser Asn Leu Trp Ala Val Glu Gly Gly Asn Lys
             245
                     250
<210> 707
<211> 150
<212> PRT
<213> Mouse
<400> 707
Met Ser Trp Trp Arg Asp Asn Phe Trp Ile Ile Leu Ala Met Ser Ile
                   10
Ile Phe Ile Ser Leu Val Leu Gly Leu Ile Leu Tyr Cys Val Cys Arg
 20
                            25
                                            30
Trp Gln Leu Arg Gln Gly Arg Asn Trp Glu Ile Ala Lys Pro Ser Lys 35 40 45
Gln Asp Gly Arg Asp Glu Glu Lys Met Tyr Glu Asn Val Leu Asn Ser 50 60^{\circ}
Ser Pro Gly Gln Leu Pro Ala Leu Pro Pro Arg Gly Ser Pro Phe Pro
                70
                                75
Gly Asp Leu Ala Pro Gln Glu Ala Pro Arg Gln Pro Ser Ala Trp Tyr
           85
                   90
Ser Ser Val Lys Lys Val Arg Asn Lys Lys Val Phe Ala Ile Ser Gly
100 105 110
Ser Thr Glu Pro Glu Asn Asp Tyr Asp Asp Val Glu Ile Pro Ala Thr
 115 120 125
Thr Glu Thr Gln His Ser Lys Thr Thr Pro Phe Trp Gln Ala Glu Val
Gly Leu His Ser Ser Phe
145
       150
<210> 708
<211> 114
<212> PRT
<213> Mouse
Met Phe Leu Val Tyr Phe Ser Arg Arg Gly His Cys Ile Asn Tyr Val
                                10
                                                  15
Lys Gly His Ala Asp Ser Leu Ala Pro Trp Cys Cys Gly Val Gly Leu
 20
                           25
Arg Ser Pro Leu Ala Arg Pro Gln His Gly His Val Ser Pro Lys Asp 35 40 45
His Val Pro Gly Gly His Ala Pro Gly Pro Ser His Lys Trp Leu Cys
 50
                 55
                                   60
Thr Ala Ala Leu Trp Arg Tyr Leu Glu His Ser Ala Val Thr His Gly
                70
                          75 . 80
Thr Ala Leu Pro Glu Ala His Ala Val Arg Gly Lys His Gly Lys Lys
85 90 95
Gly Arg Arg Val Val Cys Cys Ser Val Asp Phe Pro Gln Ala Thr Ser
                            105.
```

Leu Phe

```
<210> 709
<211> 132
<212> PRT
<213> Mouse
<400> 709
Ala His Pro Arg Pro Gly Ala Arg Pro Arg Leu Leu Ala Phe Gln
1 5 1.0
Ala Ser Cys Ala Pro Ala Pro Gly Ser Arg Asp Arg Cys Pro Glu Glu
        20
                             25
                                               30
Gly Gly Pro Arg Cys Leu Arg Val Tyr Ala Gly Leu Ile Gly Thr Val 35 40
Val Thr Pro Asn Tyr Leu Asp Asn Val Ser Ala Arg Val Ala Pro Trp 50 55 60
Cys Gly Cys Ala Ala Ser Gly Asn Arg Arg Glu Glu Cys Glu Ala Phe 65 70 75 80
               70
                                  75
Arg Lys Leu Phe Thr Arg Asn Pro Cys Leu Asp Gly Ala Ile Gln Ala
                       90 . 95
Phe Asp Ser Leu Gln Pro Ser Val Leu Gln Asp Gln Thr Ala Gly Cys 100 105 110
Cys Phe Pro Arg Val Ser Trp Leu Tyr Ala Leu Thr Ala Leu Ala Leu
   115
                120
Gln Ala Leu Leu
 130
<210> 710
<211> 255
<212> PRT
<213> Mouse
<400> 710
Met Arg Val Leu Trp Val Leu Gly Leu Cys Cys Val Leu Leu Thr Phe
                                10
Gly Phe Val Arg Ala Asp Asp Glu Val Asp Val Asp Gly Thr Val Glu
                            25
                                               30
Glu Asp Leu Gly Lys Ser Arg Glu Gly Ser Arg Thr Asp Asp Glu Val
35 40
Val Gln Arg Glu Glu Glu Ala Ile Gln Leu Asp Gly Leu Asn Ala Ser 50 55 60
Gln Ile Arg Glu Leu Arg Glu Lys Ser Glu Lys Phe Ala Phe Gln Ala
                 70
                                   75
Glu Val Asn Arg Met Met Lys Leu Ile Ile Asn Ser Leu Tyr Lys Asn
             85
                        90
                                                  95
Lys Glu Ile Phe Leu Arg Glu Leu Ile Ser Asn Ala Ser Asp Ala Leu
100 105 110
                            105
                                               110
Asp Lys Ile Arg Leu Ile Ser Leu Thr Asp Glu Asn Ala Leu Ala Gly
115 120 125
                      120 125
Asn Glu Glu Leu Thr Val Lys Ile Lys Cys Asp Lys Glu Lys Asn Leu
130 140
Leu His Val Thr Asp Thr Gly Val Gly Met Thr Arg Glu Glu Leu Val
145
               150 155 . 160
Lys Asn Leu Gly Thr Ile Ala Lys Ser Gly Thr Ser Glu Phe Leu Asn 165 170 175
Lys Met Thr Glu Ala Gln Glu Asp Gly Gln Ser Thr Ser Glu Leu Ile
```

```
180
                        185
                                        190
Gly Gln Phe Gly Val Gly Phe Tyr Ser Ala Phe Leu Val Ala Asp Lys
  195
             200
                             205
Val Ile Val Thr Ser Lys His Asn Asn Asp Thr Gln His Ile Trp Glu
 210 215 220
Ser Asp Ser Asn Glu Phe Ser Val Ile Ala Asp Pro Arg Gly Asn Thr
                      235
225 230
Leu Gly Arg Gly Thr Thr Ile'Thr Leu Val Leu Lys Glu Glu Ala
 245 250 255
<210> 711
<211> 224
<212> PRT
<213> Mouse
<400> 711
Met Ala Leu Leu Ile Ser Leu Pro Gly Gly Thr Pro Ala Met Ala Gln
1 5 10
Val Leu Leu Leu Ser Ser Gly Cys Leu His Ala Gly Asn Ser Glu
       20
                        25
                                      30
Arg Tyr Asn Arg Lys Asn Gly Phe Gly Val Asn Gln Pro Glu Arg Cys
    35
                   40
Ser Gly Val Gln Gly Gly Ser Ile Asp Ile Pro Phe Ser Phe Tyr Phe 50
Pro Trp Lys Leu Ala Lys Asp Pro Gln Met Ser Ile Ala Trp Lys Trp
             70
                        75
Lys Asp Phe His Gly Glu Val Ile Tyr Asn Ser Ser Leu Pro Phe Ile
           85
                90
His Glu His Phe Lys Gly Arg Leu Ile Leu Asn Trp Thr Gln Gly Gln 100 105 110
Thr Ser Gly Val Leu Arg Ile Leu Asn Leu Lys Glu Ser Asp Gln Ala
   115 120
                         125
Gln Tyr Phe Ser Arg Val Asn Leu Gln Ser Thr Glu Gly Met Lys Leu
130 135 140
Trp Gln Ser Ile Pro Gly Thr Gln Leu Asn Val Thr Gln Ala Leu Asn 145 150 150 155 160
Thr Thr Met Arg Ser Pro Phe Ile Val Thr Ser Glu Phe Thr Thr Ala
165 170 175
Gly Leu Glu His Thr Ser Asp Gln Arg Asn Pro Ser Leu Met Asn Leu
 180 185 190
Gly Ala Met Val Thr Met Leu Leu Ala Lys Val Leu Val Ile Val Leu
  195 200 205
Val Tyr Gly Trp Met Ile Phe Leu Arg Trp Lys Gln Arg Pro Ala His
               215
<210> 712
<211> 133
<212> PRT
<213> Mouse
<400> 712
Met Ala Leu Pro Trp Thr Ile Leu Leu Ala Leu Ser Gly Ile Tyr Val
         5 10 . 15
Gln Gly Ala Gln Ala Trp Cys Ser Glu Glu Asp Thr Leu Glu Leu Asp
  20
                  25
Lys Leu Val Ser Glu Pro Asp Ile Val Lys Phe Ala Leu Ser Ala Phe
   35
                    40,
                                    45
```

```
His Lys Lys Ser Lys Asp Glu Tyr Ala Tyr Arg Val Ile His Ile Met 50 60
Asn Phe Leu Lys Val Gln Glu Glu Pro Pro Gln Thr Phe Phe Val Lys 65 70 75 80
Leu Arg Leu Thr Arg Thr Ile Cys Met Lys Phe Glu Lys Ser Leu Asp
85 90 95
Thr Cys Pro Leu Pro Glu Leu Gln Asn Ile Leu Ile Cys Ser Phe Ser 100 105 110
Ile Ser Ser Pro Gly Ser Lys Gln Phe Asn Leu Leu Lys Met Thr Cys
 115 120
Ser Glu Gly Leu Leu
130
<210> 713
<211> 255
<212> PRT
<213> Mouse
<400> 713
Cys Asp Lys Phe Arg Ala Lys Gly Arg Lys Pro Cys Lys Leu Met Leu
20 25
                            25
Gln Val Val Lys Ile Leu Val Val Thr Val Gln Leu Ile Leu Phe Gly
 35 - 40
Leu Ser Asn Gln Leu Val Val Thr Phe Arg Glu Glu Asn Thr Ile Ala
50 55
                                  60
Phe Arg His Leu Phe Leu Leu Gly Tyr Ser Asp Gly Ser Asp Asp Thr 65 70 75 80
                                75
Phe Ala Ala Tyr Thr Gln Glu Gln Leu Tyr Gln Ala Ile Phe Tyr Ala
           85 90 95 .
Val Asp Gln Tyr Leu Ile Leu Pro Glu Ile Ser Leu Gly Arg Tyr Ala
100 105 110 110
Tyr Val Arg Gly Gly Gly Gly Pro Trp Ala Asn Gly Ser Ala Leu Ala 115 120 125
Leu Cys Gln Arg Tyr Tyr His Arg Gly His Val Asp Pro Ala Asn Asp
 130 135 140
Thr Phe Asp Ile Asp Pro Arg Val Val Thr Asp Cys Ile Gln Val Asp 145 150 155 160
Pro Pro Asp Arg Pro Pro Asp Ile Pro Ser Glu Asp Leu Asp Phe Leu
      165 170 175
Asp Gly Ser Ala Ser Tyr Lys Asn Leu Thr Leu Lys Phe His Lys Leu
180 185 190
Ile Asn Val Thr Ile His Phe Gln Leu Lys Thr Ile Asn Leu Gln Ser
195 200 205
Leu Ile Asn Asn Glu Ile Pro Asp Cys Tyr Thr Phe Ser Ile Leu Ile
 210 215 220 __,
Thr Phe Asp Asn Lys Ala His Ser Gly Arg Ile Pro Ile Arg Leu Glu 225 230 240
Thr Lys Thr His Ile Gln Glu Cys Lys His Pro Ser Val Ser Arg
             245
                               250 255
<210> 714
<211> 255
<212> PRT
<213> Mouse
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```
<400> 714
Met Asn Ile Val Val Glu Phe Phe Val Val Thr Phe Lys Val Leu Trp
                           10
Ala Phe Val Leu Ala Ala Ala Arg Trp Leu Val Arg Pro Lys Glu Lys
    20 25 30
Ser Val Ala Gly Gln Val Cys Leu Ile Thr Gly Ala Gly Ser Gly Leu
                    40
                                    45
Gly Arg Leu Phe Ala Leu Glu 'Phe Ala Arg Arg Arg Ala Leu Leu Val
       55
Leu Trp Asp Ile Asn Thr Gln Ser Asn Glu Glu Thr Ala Gly Met Val
65 70 75
Arg His Ile Tyr Arg Asp Leu Glu Ala Ala Asp Ala Ala Ala Leu Gln
                         90
                                         95
Ala Gly Lys Gly Glu Glu Glu Ile Leu Pro Pro Cys Asn Leu Gln Val
        100
                105
Phe Thr Tyr Thr Cys Asp Val Gly Lys Arg Glu Asn Val Tyr Leu Thr 115 120 125
Ala Glu Arg Val Arg Lys Glu Val Gly Glu Val Ser Val Leu Val Asn
 130
               135
                           140
Asn Ala Gly Val Gly Ser Gly His His Leu Leu Glu Cys Pro Asp Glu
    150
                      155 160
Leu Ile Glu Arg Thr Met Met Val Asn Cys His Ala His Phe Trp Thr
165 170 175
Thr Lys Ala Phe Leu Pro Thr Met Leu Glu Ile Asn His Gly His Ile
        180 185 190
Val Thr Val Ala Ser Ser Leu Gly Leu Phe Ser Thr Ala Gly Val Glu
   195 200 205
Asp Tyr Cys Ala Ser Lys Phe Gly Val Val Gly Phe His Glu Ser Leu 210 215 220
Ser His Glu Leu Lys Ala Ala Glu Lys Asp Gly Ile Lys Thr Thr Leu
225 230 235
Val Cys Pro Tyr Leu Val Asp Thr Gly Met Phe Arg Gly Cys Arg
245
                           250
                                           255
<210> 715
<211> 200
<212> PRT
<213> Mouse
<400> 715
Met Phe Pro Lys Asn Ser Arg Cys Pro Thr Cys Asp Leu Arg Lys Pro
1 5 10
Ala Arg Ser Lys His Cys Arg Leu Cys Asp Arg Cys Val His Arg Phe
      20
                      25
Asp His His Cys Val Trp Val Asn Asn Cys Ile Gly Ala Trp Asn Thr
             40
                                   45
Arg Tyr Phe Leu Ile Tyr Leu Leu Thr Leu Thr Ala Ser_Ala Ala Thr
                         60
 50 55
Ile Ala Thr Val Thr Ala Ala Phe Leu Leu Arg Leu Val Thr Val Ser
             70
                      75
Asp Leu Tyr Gln Glu Thr Tyr Leu Asp Asp Val Gly His Phe Gln Ala
                          90 . 95
         85
Val Asp Thr Val Phe Leu Ile Gln His Leu Phe Leu Ala Phe Pro Arg
1.1.5
                 120 125
Gly Tyr Leu Cys Phe Ala Leu Tyr Leu Ala Ala Thr Asn Gln Thr Thr
```

```
130
                   135
                                     140
Asn Glu Trp Tyr Lys Gly Asp Trp Ala Trp Cys Gln Arg Trp Pro Leu
145 150 155 160
Val Ala Trp Ser Pro Ser Ala Glu Pro Arg Ile His Gln Asn Ile His
          165 170 175
Ser His Gly Phe Arg Ser Asn Leu Arg Glu Ile Phe Leu Pro Ala Thr 180 185 190
Pro Ser Tyr Lys Lys Lys Glu'Lys
     195 . 200
<210> 716
<211> 115
<212> PRT
<213> Mouse
<400> 716
Gly Glu Leu Arg Ala Leu Leu Ala Phe Thr His Leu Ser Ser Ala His
1 5
                             10
Phe Trp Leu Met Met Thr Leu Gly Gly Leu Phe Gly Phe Ala Ile Gly
 20
                    25
                                         30
Tyr Val Thr Gly Leu Leu Ile Lys Phe Thr Ser Pro Leu Thr His Asn 35 40 45
   35
                      40
                                       45
Val Ser Gly Thr Ala Lys Ala Cys Ala Gln Thr Val Leu Ala Val Leu
50 55 60
Tyr Tyr Glu Glu Ile Lys Ser Phe Leu Trp Trp Thr Ser Asn Leu Met
              70
                                 75
Val Leu Gly Gly Ser Ser Ala Tyr Thr Trp Val Arg Gly Trp Glu Met
85 90
Gln Lys Thr Gln Glu Asp Pro Ser Ser Lys Asp Gly Glu Lys Ser Ala
               105
                                    110
Ile Arg Val
 115
<210> 717
<211> 88
<212> PRT
<213> Mouse
<400> 717
Met Lys Ile Pro Ile Leu Pro Val Val Ala Leu Leu Ser Leu Leu Ala
           5
                           10
Leu His Ala Val Gln Gly Ala Ala Leu Gly His Pro Thr Ile Tyr Pro
20 25
Glu Asp Ser Ser Tyr Asn Asn Tyr Pro Thr Ala Thr Glu Ala Phe Gln
35
                40
Ser Glu Asn Phe Leu Asn Trp His Val Ile Thr Asp Met Phe Lys Asn 50 55 60 ...
Ala Phe Pro Phe Ile Asn Trp Asp Phe Phe Pro Lys Val Lys Gly Leu
65 70
                             75
Arg Ser Ala Ala Pro Asp Ser Gln
             85
<210> 718
<211> 84
<212> PRT
<213> Mouse
```

```
<400> 718
Met Arg Leu Pro Ile Phe His Ile Ile Ala Phe Phe Leu Val Val
              5
                            10
Ser Met Gly Cys Thr Cys Ala His Gly Gly Gln Arg Ser Asp Leu Cys
  20
                   25
Thr Cys Gly Tyr Met Glu Val Arg Gly His Val Arg Arg Leu Leu Leu 45
Leu Phe Ser Thr Phe Lys Arg Ile Val Ile Glu Ala Glu Gly Gly 50 55
                             60
Met Gly Trp Gly Gly Leu Gln Arg Gly Asn Arg Glu Gly Gly Gln His
Leu Lys Cys Lys
<210> 719
<211> 135
<212> PRT
<213> Mouse
<400> 719
Met Phe Val Ala Phe Tyr Ile Cys Thr Phe Leu Met Arg Phe Val Ser
1.
                             10
Thr Pro Val Thr Arg Met Cys Cys Pro Arg Gly Asp Ala Ala Trp Arg
 20
                         25
Arg Pro Tyr Pro Leu Pro Leu Asp Leu Phe Gly Gly Thr Pro Ser Pro 35 40
                 40
Gly Pro Gly Ala Gly Arg Gly Ala Ser Cys Arg Pro Gln Ala Tyr Ser 50 55 60
Glu Leu Val Phe Leu Lys Val Phe Leu Asp Pro Val Leu Val Asn Ile
              70 75 80
Ser Ile Ile Leu Thr Arg Ala Ser Ser Cys Ser Leu Ser Leu
           85
                           90
                                           95
Leu Thr Lys Phe Ile Val Ala Ile Lys Val Phe Tyr Phe Pro Val His
 115 120
Ile Thr Leu Val Ser Ser Pro
. 130 135
<210> 720
<211> 129
<212> PRT
<213> Mouse
<400> 720
Met Ile Arg Ile Phe Val Leu Phe Val Phe Trp Phe Leu Ile Tyr As\mathfrak{p} 1 10 15 15
                10 ____, 15
Ser Pro Thr His Leu Tyr Leu Phe Ile Phe Phe Ser Leu Phe Leu Gly
20
                         25 30
Lys Pro Asp Leu Leu His Pro Gln Ala Ile Pro Pro Ala Ser Leu Gly
 35
                   40
                                     45
Gly Pro Leu Gly Leu Pro Cys Ala Pro Val Cys Pro Gly Leu Ala 50 55 60
Arg Leu Ser Pro Pro Ala Arg Gly Ser Ser Arg Ala Leu Met Val Leu
              70 75 80
Lys Pro Ala Pro Leu Pro Tyr Val Leu His Phe Leu Gly Pro Val Pro
```

, 90

85

```
Pro Leu Pro Thr Gln Pro Arg Pro His Leu Arg Val Ser Asp Ser Cys
    100 105 110
Thr Val Gly Glu Glu Val Gly Thr Glu Met Val Phe Cys Lys Lys Asn
               120
                                         125
       115
<210> 721
<211> 255
<212> PRT
<213> Mouse
<400> 721
Met Ser Trp Glu Leu Leu Leu Trp Leu Leu Ala Leu Cys Ala Leu Ile
          5 10
Leu Pro Leu Val Gln Leu Leu Arg Phe Leu Arg Ala Asp Ala Asp Leu 20 25 30
Thr Leu Leu Trp Ala Glu Trp Gln Gly Arg Arg Pro Glu Trp Glu Leu
                       40
                                       45
Thr Asp Met Val Val Trp Val Thr Gly Ala Ser Ser Gly Ile Gly Glu
50 55 60
Glu Leu Ala Phe Gln Leu Ser Lys Leu Gly Val Ser Leu Val Leu Ser 65 70 Fe 75 80
Ala Arg Arg Ala Gln Glu Leu Glu Arg Val Lys Arg Arg Cys Leu Glu
85 90 95
Asn Gly Asn Leu Lys Glu Lys Asp Ile Leu Val Leu Pro Leu Asp Leu
        100 105 110
Thr Asp Thr Ser Ser His Glu Ala Ala Thr Lys Ala Val Leu Gln Glu 115 120 125
Phe Gly Lys Ile Asp Ile Leu Val Asn Asn Gly Gly Arg Ser Gln Arg
130 135 140
Ser Leu Val Leu Glu Thr Asn Leu Asp Val Phe Lys Glu Leu Ile Asn
145 150 155 160
Leu Asn Tyr Ile Gly Thr Val Ser Leu Thr Lys Cys Val Leu Pro His
165 170 175
Met Ile Glu Arg Lys Gln Gly Lys Ile Val Thr Val Asn Ser Ile Ala
  180 185 190
Gly Ile Ala Ser Val Ser Leu Ser Ser Gly Tyr Cys Ala Ser Lys His
195 200 205
Ala Leu Arg Gly Phe Phe Asn Ala Leu His Ser Glu Leu Gly Gln Tyr 210 215 220
Pro Gly Ile Thr Phe Cys Asn Val Tyr Pro Gly Pro Val Gln Ser Asp
225 230 235 240
Ile Val Lys Asn Ala Phe Thr Glu Glu Val Thr Lys Ser Met Arg
          245
                               250
                                       255
<210> 722
<211> 115
<212> PRT
<213> Mouse
<400> 722
Asp Asp Ser Thr Tyr Cys Asp Tyr Lys Leu Thr Phe Ile Val His Ile

1 10 15
His Gly Leu Pro Leu Ser Ser Lys Gln Ser Ser Phe Ile Val Met Val
       20
                       25 30
Ser Thr Ser Phe Phe Ile Ala Leu Val Val Phe Tyr Ile Leu Phe Cys
```

```
40
Leu Leu Trp Pro Arg Ile Val Lys Ala Trp Val Ser Phe Arg Trp Lys 50 55 60
Ile His Asn Met Met Ala Pro Glu Thr Tyr Ser Ser Ser Ser Ser Ser
65 70
                                 75
Gly Gly Phe Thr Leu His Ser His Ser Ser Glu Gly Ser Phe Glu Gly
                           90
        85
Pro Ser Arg Pro Gly Thr Lys Glu Asp Asn Val Gln Ala Lys Arg Ala
         100
                  105
Lys Val Ala
115
<210> 723
<211> 145
<212> PRT
<213> Human
<400> 723
Met Cys Tyr Gly Lys Cys Ala Arg Cys Ile Gly His Ser Leu Val Gly
                               10
Leu Ala Leu Leu Cys Ile Ala Ala Asn Ile Leu Leu Tyr Phe Pro Asn
         20
                            25
                                              30
Gly Glu Thr Lys Tyr Ala Ser Glu Asn His Leu Ser Arg Phe Val Trp
     35
                        40
Phe Phe Ser Gly Ile Val Gly Gly Leu Leu Met Leu Leu Pro Ala
50 55
                                 . 60
Phe Val Phe Ile Gly Leu Glu Gln Asp Asp Cys Cys Gly Cys Cys Gly 65 70 75 80
                 70
                                   75
His Glu Asn Cys Gly Lys Arg Cys Ala Met Leu Ser Ser Val Leu Ala
                              90
Ala Leu Ile Gly Ile Ala Gly Ser Gly Tyr Cys Val Ile Val Ala Ala
         100
                           105
                                              110
Leu Gly Leu Ala Glu Gly Pro Leu Cys Leu Asp Ser Leu Gly Gln Trp
115 120 125
                     120
Asn Tyr Thr Phe Ala Ser Thr Glu Gly Gln Tyr Leu Gly Arg Asp His
130
            135
Ala
145
<210> 724
<211> 217
<212> PRT
<213> Mouse
<400> 724
Met Glu Ala Gly Arg Arg Gly Ala Ala Leu Gly Asp Leu Val Pro Ser 1 5 10 10 . . . 15
Arg Pro Pro Ser Phe Ser Pro Cys Pro Ala Glu Asp Leu Phe Pro Gly
                         25
   20
Arg Arg Tyr Asp Gly Gly Leu Asp Ser Gly Phe His Ser Val Asp Ser
    35
                       40
                                        45
Gly Ser Lys Arg Trp Ser Gly Asn Glu Ser Thr Asp Asp Phe Ser Glu
                   55
                                     60 ·
Leu Ser Phe Arg Ile Ser Glu Leu Ala Arg Asp Pro Arg Gly Pro Arg
               70 75
Gln Pro Arg Glu Asp Gly Ala Gly Asp Gly Asp Leu Glu Gln Ile Asp
```

85

, 90

```
Phe Ile Asp Ser His Val Pro Gly Glu Asp Glu Asp Arg Ser Ala Ala 100 105
Glu Glu Gln Leu Pro Ser Glu Leu Ser Leu Val Ala Gly Asp Val Glu
 115 120
                                 125
Lys Pro Ser Ser Arg Arg Glu Glu Pro Ala Gly Glu Glu Arg Arg
 130 135 140
Arg Pro Asp Thr Leu Gln Leu Trp Gln Glu Arg Glu Arg Lys Gln Gln 145 150 155 160
Gln Gln Ser Gly Gly Trp Gly Ser Pro Arg Lys Asp Ser Val Leu Lys
165 170 175
Arg Gly Ile Arg Ala Ala Gly Ala Gly Ala Ser Ala Pro Ser Thr Gln
180 185 190
Ala Thr Cys Asn Gly Pro Pro Pro Arg Thr Pro Phe Leu Tyr Leu Asp
195 200 205
                                  205
Gln Val Leu Pro Leu Gln Ser Leu Phe
                     215
<210> 725
<211> 255
<212> PRT
<213> Mouse
<400> 725
Met Leu Pro Arg Gly Arg Pro Arg Ala Met Gly Ala Ala Val Leu Leu
1 5
                              10
Leu Leu Leu Leu Val Val Gly Phe Phe Leu Phe Gly Arg Asp Pro
 20
                             25
Asp Tyr Gly Leu Gly Thr Thr Ala Thr Leu Asp Glu Asp Pro Tyr Arg 35 40 45
Ser Arg Asn Leu Ser Ala Ser Ser Pro Gln Leu Leu Leu Pro Pro Lys 50 55
Cys Glu Met Leu His Val Ala Ile Val Cys Ala Gly Tyr Asn Ser Ser 65 70 75 80
Arg Glu Ile Ile Thr Leu Thr Lys Ser Leu Leu Phe Tyr Arg Lys Asn 85 90 95
Pro Leu His Leu His Leu Ile Thr Asp Ala Val Ala Arg Asn Ile Leu 100 105 110
Glu Thr Leu Phe Arg Thr Trp Met Val Pro Ala Val Val Ser Phe
     115
                      120 125
Tyr Asp Ala Glu Glu Leu Lys Pro Leu Val Ser Trp Ile Pro Asn Lys
130 140
His Tyr Ser Gly Leu Tyr Gly Leu Met Lys Leu Val Leu Pro Ser Ile
145 155 160
Leu Pro Pro Ser Leu Ala Arg Val Ile Val Leu Asp Thr Asp Val Thr 165 170 175
Phe Ser Ser Asp Ile Val Glu Leu Trp Ala Leu Phe Asp His Phe Ser
        180 185 - 190
Asp Lys Gln Val Val Gly Leu Val Glu Asn Gln Ser Asp Trp Tyr Leu
195 200 205
Gly Asn Leu Trp Lys Asn His Arg Pro Trp Pro Ala Leu Gly Arg Gly
 21.0
                  215 220
Phe Asn Thr Gly Val Ile Leu Leu Trp Leu Asp Arg Leu Gln Gln Thr
225 230 235 240
Gly Trp Glu Gln Met Trp Lys Val Thr Ala Lys Arg Glu Leu Leu
                              250
              245
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International application No.

			PCT/NZ01/00099	
Α.	CLASSIFICATION OF SUBJECT MATTER			
Int. Cl. 7:	C12N 15/12, 15/18, 15/19			
According to	International Patent Classification (IPC) or to both	national classification and II	PC	
В.	FIELDS SEARCHED			
Minimum doci	umentation searched (classification system followed by c	classification symbols)		
AS BELOW				
	base consulted during the international search (name of ss Prot, EMBL, Genebank, : SEQ ID. NOS. 1		le, search terms used)	
C. DOCUMENTS CONSIDERED TO BE RELEVANT				
Category*	Citation of document, with indication, where app	propriate, of the relevant pass	sages Relevant to claim No.	
P, X	EP 1 067 182 HELIX RESEARCH INSTITUTE Sequence Id. 487, & GeneBank Accession N		ee 1 - 3. (SEQ ID NO 1)	
P, X	EP 1067 182 HELIX RESEARCH INSTITU Sequence Id. 219, & GeneBank Accession N		te 1 - 3. (SEQ ID NO 1)	
Х	EMBL Accession Number AC008119 (9 Oc 12q24.1-116.6-118.9 BAC RPCI11-951I11	ctober 1999) Homo sapien	1 - 3. (SEQ ID NO 1)	
X Further documents are listed in the continuation of Box C X See patent family annex				
* Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention document of particular relevance; the claimed invention cannot document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is taken alone document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art document member of the same patent family				
Determine the state of the state of the state of the state of course we can be seen that the state of the sta		tional search report 200/		
Name and mailing address of the ISA/AU Authorized officer AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929 ALISTAIR BESTOW Telephone No: (02) 6283 2450			 2450	

International application No.

PCT/NZ01/00099

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT				
		T		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.		
X	US, A, 5 952 486 L. N. BLOKSBERG ET. AL. (14 September 1999) See SEQ ID 53. & GeneBank Accession number AR074144.	1 - 3. (SEQ ID NO 2)		
X	WO, A, 2000 40752 THE NOTTINGHAM TRENT UNIVERSITY (13 July 2000) See SEQ ID NO. 2. & GeneBank Accession Number AX026540.	1 - 3. (SEQ ID NO 2)		
X	EMBL Accession Number UCAJ4935 (2 March 1999.) Urechis caupo mRNA for cytoplasmic intermediate filament protein.	1 - 3. (SEQ ID NO 2)		
x	WO, A, 99 53040 METAGEN GESELLSCHAFT FÜR GENOMFORSCHUNG MBH (21 October 1999) See SEQ ID 31. & GenBank Accession Number AX014842.	1 - 3. (SEQ ID NO 4)		
P, X	WO, A, 2001 07612 INCYTE GENOMICS, INC. (1 February 2001) See SEQ ID 43 & Genebank Accession Number AX078375.	1 - 3. (SEQ ID NO 4)		
P, X	WO, A, 2001 10902 CURAGEN CORPORATION (15 February 2001) See SEQ ID 5 & Genebank Accession Number AX084211.	1 - 3. (SEQ ID NO 5)		
x	EMBL Accession Number AF169677 (29 JANUARY 2000) Homo sapiens leucine-rich repeat transmembrane protein FLRT3 (FLRT3) mRNA, complete cds.	1 - 3. (SEQ ID NO 5)		
X	EMBL Accession Number RNMOG (20 August 1992) Rattus norvegicus myelin/oligodendrocyte glycoprotein (MOG) gene, complete cds.	1 - 3. (SEQ ID NO 7)		
A	EMBL Accession Number D50030 (14 April 2000) Homo sapiens gene for hepatocyte growth factor activator, complete cds.	1 - 3. (SEQ ID NO 8)		
Х	WO, A, 99 55865 GENESIS RESEARCH AND DEVELOPMENT CORPORATION LIMITED (4 November 1999) See SEQ ID NOS 1 - 10, 147, 187, 196, 294, 295 and 395.	1 - 3, 8-17, 27-29 (SEQ ID NOS 1-10, 147, 196, 294, 295, 413-5, 417)		
P, X	WO, A, 2000 69884 GENESIS RESEARCH AND DEVELOPMENT CORPORATION LIMITED (23 November 2000) See SEQ ID NOS 1 - 10, 147, 187, 196, 294, 295 and 395.	1 - 3, 8-17, 27-29 (SEQ ID NOS 1-10, 147, 196, 294, 295, 413-5, 417)		

International application No. PCT/NZ01/00099

	PCT/NZ01/	00033		
C (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT				
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.		
PX	WO, A, 00 63230 HUMAN GENOME SCIENCES, INC. (26 October 2000) See SEQ ID NO 68 and pages 16-29	1-3, 8-17, 27- 29 (SEQ ID NOS 196, 413-5, 417		
х	WO, A, 00 29438 MILLENNIUM PHARMACEUTICALS, INC. (25 May 2000) See Figures 1, 3, 5,7 and 8	1-3, 8-17, 27 29 (SEQ ID NOS 196, 413-5, 417		
PX	WO, A, 00 63377 ZYMOGENETICS, INC. (26 October 2000) See SEQ ID NOS 1 and 11	1-3 (SEQ ID NO 147, 294		
PX	WO, A, 01 49728 PROTOGENE, INC. (12 July 2001) See SEQ ID NO 59 and Table 1	1-3 (SEQ ID NO 147)		
PX	WO, A, 00 73448 ZYMOGENETICS, INC. (7 December 2000) See SEQ ID NOS 1 and 14	1-3 (SEQ ID NO 294)		
X	GenPept Accession No. CAB53702 (18 February 2000) Hypothetical Protein Homo sapiens Ottenwaelder B et al	1-3 (SEQ ID NO 295)		

International application No.

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Box I	Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)			
This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:				
1.	Claims Nos:			
	because they relate to subject matter not required to be searched by this Authority, namely:			
2.	Claims Nos: because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:			
3.	Claims Nos: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a)			
Box II	Observations where unity of invention is lacking (Continuation of item 3 of first sheet)			
This International Searching Authority found multiple inventions in this international application, as follows:				
1.	As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims			
2.	As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.			
3.	report covers only those claims for which fees were paid, specifically claims Nos.:			
	1-3, 8-17 and 27-29 (SEQ ID NOS 1-10, 147, 196, 294, 295, 413-415, 417)			
	More than one invention has been claimed. (continued in supplemental box			
4.	No required additional search fees were timely paid by the applicant.			
Remark on	Protest The additional search fees were accompanied by the applicant's protest. X No protest accompanied the payment of additional search fees.			

International application No.

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Supplemental Box

(To be used when the space in any of Boxes I to VIII is not sufficient)

Continuation of Box No: II

Rule 13.1 of the PCT states the principle that an International Application should relate to only one invention or, if there is more than one invention, that the inclusion of those inventions in one International Application is only permitted if all inventions are so linked to form a single general inventive concept. Rule 13.2 of the PCT defines the method for determining whether the requirement of unity of invention is satisfied in respect of a group of inventions claimed in the International application. Unity of invention exists only when there is a technical relationship among the claimed inventions involving one or more of the same or corresponding "special technical features." The expression "special technical features" is defined in Rule 13.2 as meaning those technical features that define a contribution which each of the inventions, considered as a whole, makes over the prior art. The determination is made on the contents of the claims as interpreted in the light of the description and drawings (if any).

There is no special technical feature which is common to all 725 sequences disclosed in the specification. It is well known in the art that for a given cell type, the cell will express a great many sequences, each having a different function from the others. That they are sourced from skin cells is not a special technical feature. For applications claiming nucleotides and peptides, there are two features which are to be considered for the purposes of determining the number of inventions in a specification.

1) If the polynucleotide has a corresponding peptide, then the two sequences may have a common special technical feature because the nucleotide encodes the peptide. Therefore they are regarded as a single invention.

In the present case, the specification does not disclose a complete concordance between the polynucleotides and corresponding polypeptides, other than those disclosed in Table 2. While Table 2 purports to provide a concordance between nucleotides and peptides for which they code, this is incomplete, as the majority of sequences are not referred to on this table. Therefore the ISA is unable to confidently determine the number of inventions, on the basis of a concordance between the polynucleotides and the peptides.

2) A group of two or more nucleotides, or two or more peptides, which share a significant structural element. A "significant structural element" is the structural element that defines the specific biological activity of an amino acid sequence or a nucleotide sequence or its encoded polypeptide and is disclosed as the feature that defines the contribution which each of the inventions, considered as a whole, makes over the prior art. If each of the inventions shares the same significant structural element, then it provides the special technical feature which is required to establish unity of invention.

In the present case, genes and their expressed proteins from skin cells have been sequenced. The applicant has provided no evidence that the nucleotide sequences of the present application, and the peptides they express, all form a group of protein types sharing a significant structural element. On the contrary, the putative peptides derived from the nucleotide sequences of the application have a wide range of functions based on their similarity to known proteins. (see Table 2) At best, it appears from Table 2 that there may be 76 distinct protein types which share a common function, and therefore may share a common significant structural element. However, most of the polynucleotides and peptides which do not appear on Table 2, have not have been identified in terms of their function, much less, whether any of them have a shared significant structural element. Therefore, the ISA is unable to confidently determine the number of inventions, on the basis of a shared significant structural element. Thus, at this stage, in the absence of a complete polynucleotide peptide concordance, or the definition of a special technical feature which is common to two or more sequences, this ISA considers that that there are 72 groupings of sequences, which encompass the 725 sequences.

While the ISA is unable to determine the precise number of inventions in this application it is prepared, as a service, to search a first group of ten sequences for a single search fee. This offer is provided purely as a service to the applicant and should not be taken as having any bearing on the ISA's assessment of the number of inventions claimed in these 10 sequences. The ISA also agrees to search the two further inventions specified by the applicant in their letter of 30 August 2001, for two additional search fees. As such, the ISA has searched SEQ ID NOS 1-10, 147, 196, 294, 295, 413-5 and 417.